Synthesis and confirmation of structure for the gibberellin GA_{131} (18-hydroxy-GA_4)

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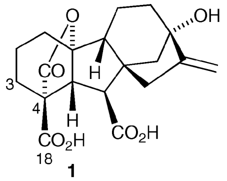
A general method for the hydroxylation of the 18-methyl group in gibberellins has been developed, as demonstrated by the successful synthesis of 18-hydroxy GA_4 (GA_{131}) by means of a tandem process involving the conjugate addition of alkoxides to the α-methylene lactone moiety of a ring A-*seco*-gibberellin followed by an intramolecular aldol reaction.

Gibberellins ("GAs") in which the 18-methyl group has undergone oxidation have been isolated from immature seeds of sword bean (*Canavalia gladiata*), *e.g.* GA_{21} (**1**) and GA_{22} (**2**),[1] and from germinating barley grain (*Hordeum vulgare*), *e.g.* 18-hydroxy GA_4 (**3**).[2] In the case of **3**, the structure was determined by converting 7β,18-dihydroxy kaurenolide (**5**) into 18-hydroxy GA_{12} and then carrying out metabolic transformation of this material to a series of 18-hydroxy C_{19} GAs with the fungus *Gibberella fujikuroi* (B1–41a mutant).[3] In order to confirm these assignments and, more importantly, provide sufficient quantities of this type of GA for more extensive biological studies, we initiated a study aimed at establishing a general procedure for the synthesis of these compounds from the fungal gibberellin, GA_4 (**4**). The successful outcome of our efforts was reported in a preliminary communication[4] as summarised in Scheme 1, the pivotal reaction being the domino process whereby the enolate anion generated by conjugate addition of an alkoxide to the unsaturated lactone **11** undergoes an intramolecular aldol reaction to afford **12**.[5,6] In this paper, we provide the full experimental details of this earlier work and describe our more recent efforts to improve the overall efficiency of the preparation.



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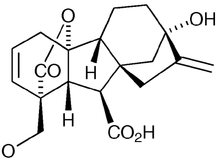

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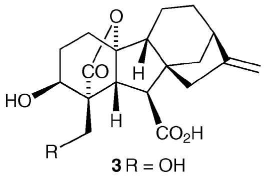

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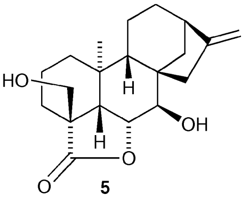
4 R = H



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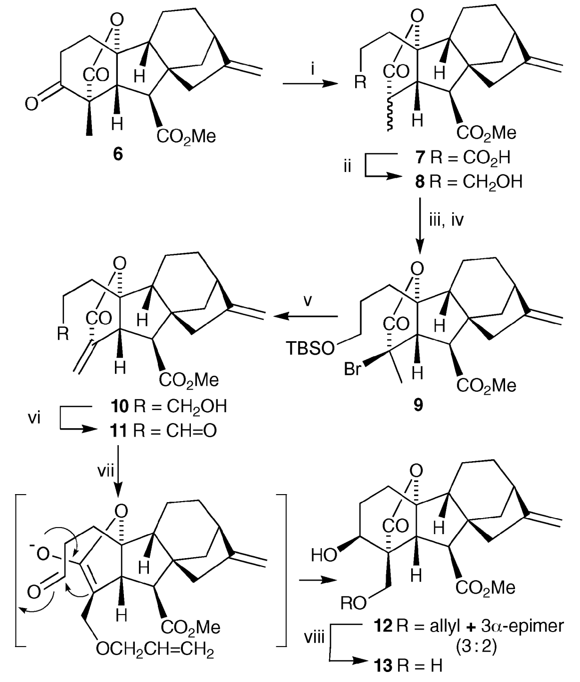

Scheme 1 Reagents and conditions: (i) 1.0 M NaOH, THF, 0 °C, 8 min, 87%; (ii) EtOCOCl, Et_3N, THF, 0 °C, then $NaBH_4$–EtOH, 70% (based on 55% conversion); (iii) TBSCl, Et_3N, imidazole, DMF, 100%; (iv) LDA, THF, −78 °C, 25 min, then CBr_4, −78 °C, 99%; (v) TBAF, THF, 0 °C to rt, 4 h, 75%; (vi) Dess–Martin periodinane, rt, 89%; (vii) K_2CO_3, allyl alcohol, rt, 80 min, 56% (3 : 2); (viii) $RhCl(PPh_3)_3$, DABCO, 10% aq. EtOH, 75 °C, 24 h, then 1.0 M HCl, rt, 30 min, 37% (based on 77% conversion).

Among other problems, considerable difficulty had been experienced in obtaining acceptable yields of alcohol **8** from activated acyl intermediates; for example, the mixed anhydride formed by treatment with ethyl chloroformate.[7] The reconstruction of the A-ring merited further attention as well and to this end we proposed to carry out the conjugate addition and aldol steps separately. Later in the sequence, liberation of the 18-hydroxyl from allyl ether **12** using $RhCl(PPh_3)_3$ and DABCO, followed by an acidic workup had afforded only modest yields of **13**.[8] The alkene bond in the D-ring places considerable constraints on the choice of reagents since, *inter alia*, it is readily hydrated or isomerised in the presence of acid. Accordingly, we chose to apply the previously established strategy to norketone **14** in the expectation that this intermediate would allow greater flexibility in the choice of reagents and reaction conditions. The modified approach is outlined in Scheme 2. The benefit of beginning with **14** (which was readily obtained from **4**

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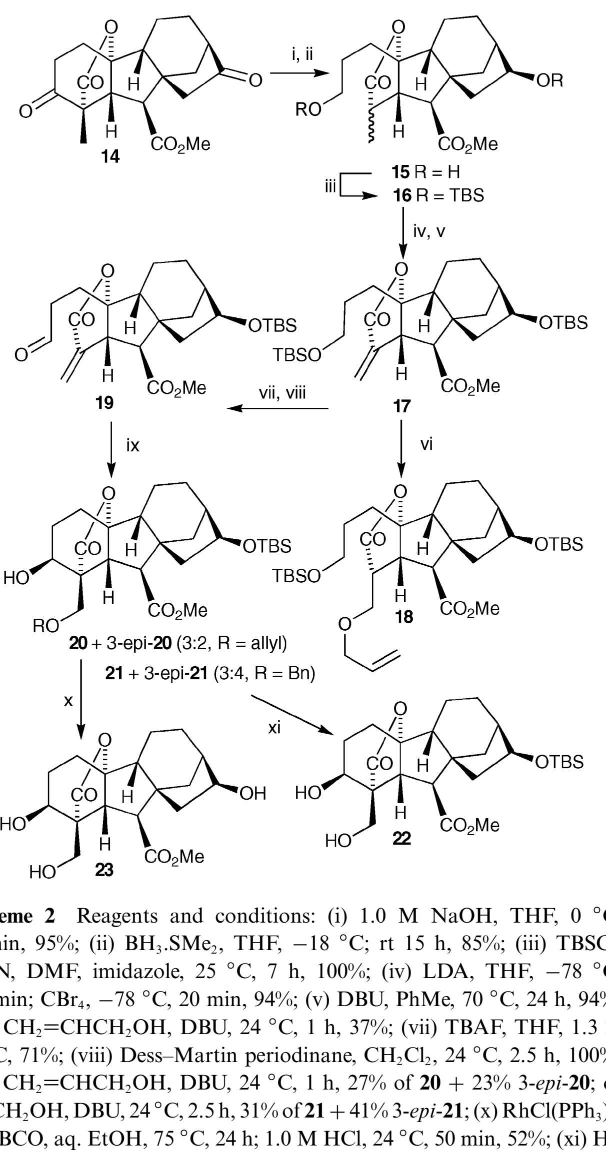
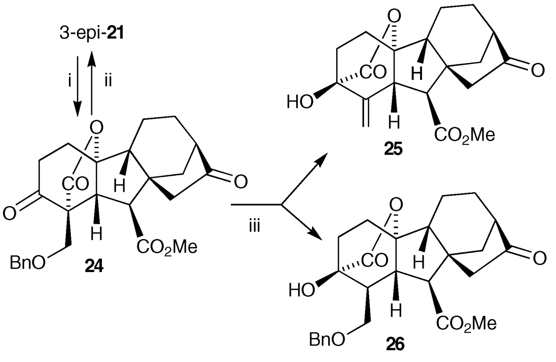


Scheme 2 Reagents and conditions: (i) 1.0 M NaOH, THF, 0 °C, 3 min, 95%; (ii) $BH_3.SMe_2$, THF, −18 °C; rt 15 h, 85%; (iii) TBSCl, Et_3N, DMF, imidazole, 25 °C, 7 h, 100%; (iv) LDA, THF, −78 °C, 25 min; CBr_4, −78 °C, 20 min, 94%; (v) DBU, PhMe, 70 °C, 24 h, 94%; (vi) $CH_2{=}CHCH_2OH$, DBU, 24 °C, 1 h, 37%; (vii) TBAF, THF, 1.3 h, 0 °C, 71%; (viii) Dess–Martin periodinane, CH_2Cl_2, 24 °C, 2.5 h, 100%; (ix) $CH_2{=}CHCH_2OH$, DBU, 24 °C, 1 h, 27% of **20** + 23% 3-*epi*-**20**; or $PhCH_2OH$, DBU, 24 °C, 2.5 h, 31% of **21** + 41% 3-*epi*-**21**; (x) $RhCl(PPh_3)_3$, DABCO, aq. EtOH, 75 °C, 24 h; 1.0 M HCl, 24 °C, 50 min, 52%; (xi) H_2, $Pd(OH)_2$, EtOAc, 72 h, 60% (based on 91% conversion).

by methylation, ozonolysis and then oxidation) was immediately realised when we came to reduce the carboxy group in the retro-Claisen product. Thus, **15** was obtained in high yield through the use of the BH_3–SMe_2 complex,[9] and although the 16-oxo function was also reduced, this change was of little consequence (see below). After protection of **15** as the bis-TBS ether **16**,[10] bromination[11] followed by treatment with DBU afforded ene-lactone **17**. With **17** in hand, we examined the conjugate addition of allyl alcohol, but obtained only a 37% yield of adduct **18** together with a similar amount of starting material. Accordingly, we reverted to the original tandem concept. When applied to aldehyde **19**, a 1.2 : 1 mixture of **20** with its 3α-epimer was obtained in a total yield of 50%. Liberation of the 18-hydroxyl was then addressed following standard protocols,[8] but we were disappointed to recover only a modest yield of very polar triol **23**, characterised as its 3,18-acetonide. Given these outcomes, we examined alternative alkoxides for the tandem operation in a search for improved yields, and were encouraged by the formation of the benzyloxy adduct **21** and its 3α-*epimer* (3 : 4 mixture, respectively) in a yield of 70%.

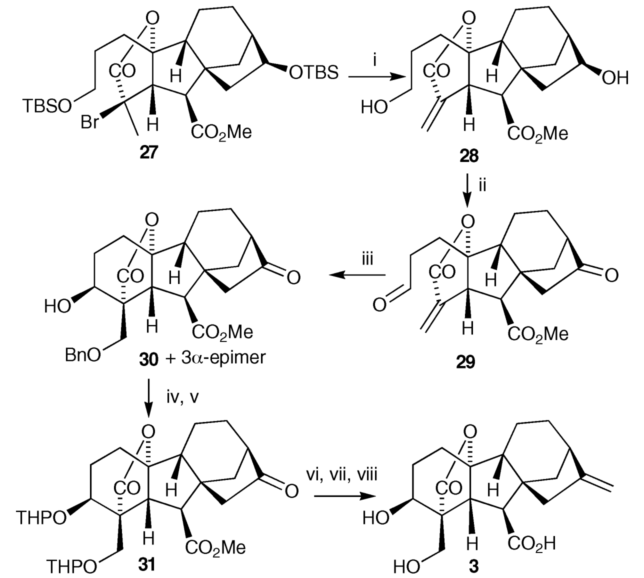
In an attempt to accumulate further amounts of the desired 3β-epimer, we examined the inversion of stereochemistry at C-3 in 3-*epi*-**21** (Scheme 3). Treatment of the derived 3-mesylate with CsOAc[12] gave mainly elimination and only 3% of the desired product, however. $NaBH_4$ reduction of the 3-oxo group in the derived ketone **24** returned mainly the 3α-ol, while reduction with SmI_2 also afforded the 3α-ol (35% yield), although this time accompanied by the rearranged hydroxy lactones **25** and **26**. The formation of these products presumably occurs by cyclisation of the intermediate C-3 ketyl radical onto the lactone carbonyl to form a cyclopropanediol, which then fragments, either with retention of the benzyloxy group, or with its elimination.



Scheme 3 Reagents and conditions: (i) Dess–Martin periodinane, CH_2Cl_2, 24 °C, 30 min, 75%; (ii) $NaBH_4$, EtOH; (iii) SmI_2, THF–H_2O: 3-*epi*-**21** (35%), **25** (9%), **26** (11%).

Ultimately, the conversion of 3-*epi*-**21** to the 3β-epimer was best achieved simply by equilibration in DBU–benzyl alcohol. This process afforded a 2 : 3 mixture of 3β- and 3α-isomers that could be separated and recycled further. Before continuing with the synthesis of **3**, we returned to the earlier stages in the synthesis in a search for greater efficiency, and were pleased to find that treatment of the bromide **27** (generated from **15**) with TBAF (Scheme 4) effected both desilylation and elimination of bromide ion to afford diol **28**. Subsequently, oxidation[13] to **29** followed by treatment with benzyl alcohol–DBU furnished a 6 : 7 mixture of **30** and its 3α-epimer in 60% yield. To complete the synthesis of 18-hydroxy GA_4 (**3**), which has now been assigned as GA_{131},[14] the benzyloxy group was subjected to hydrogenolysis and then the hydroxyl groups protected as THP ethers to afford **31**. In the case of the 3β-hydroxyl, this was undertaken to avoid epimerisation at C-3 as well as retrogression of the aldol/conjugate addition process back to **29** if exposed to strongly basic conditions. The 17-methylene group was restored by means of a Wittig reaction, then demethylation of the ester function was effected with propane thiolate,[15] after which the THP groups were removed with weak acid to afford 18-hydroxy GA_4 (**3**). Direct comparison of NMR and mass spectra with those of an authentic sample from barley confirmed the identity of the natural GA.[16,17]

The bioactivity of the synthetic sample was of considerable interest, but found to be only 25% of the parent GA_4 in a leaf growth assay.[18] Potency in the barley endosperm assay was also substantially reduced. Nevertheless, we still envisage that



Scheme 4 Reagents and conditions: (i) TBAF, THF, 12 h, 24 °C; 50 h; (ii) Dess–Martin periodinane, CH_2Cl_2, 24 °C, 60 h, 62%, 2 steps; (iii) DBU, $PhCH_2OH$, 24 °C, 3 h, 28% of **30** + 3α-epimer 32%; (iv) H_2, $Pd(OH)_2$, EtOAc, 72 h, 100%; (v) DHP, PPTS, 24 °C, 16 h, 100%; (vi) $Ph_3P{=}CH_2$, for conditions see Experimental section, 76%; (vii) PrSLi, HMPA, 24 °C, 3 h, 81%; PPTS, EtOH, 24 °C, 3 h; 57 °C, 6 h, 92%.

the attachment of auxiliary groups to C-18 might afford useful affinity probes for exploring the molecular basis of gibberellin bioactivity. To this end we have continued to develop the methodology for 18-hydroxylation and will report on those studies shortly.

Experimental

Melting points (mp) were recorded on a Gallenkamp Melting Point Apparatus and are uncorrected. Microanalyses were carried out by the Australian National University Analytical Services Unit, Canberra. Infrared (IR) spectra (ν_{max}) were recorded on a Perkin-Elmer 1800 Fourier Transform Infrared spectrophotometer as a thin film or NaCl discs. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Varian Mercury 300 spectrometer at 300 MHz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Mercury 300 spectrometer at 75.5 MHz. Distortionless enhancement by polarisation transfer (DEPT) and attached proton test (APT) experiments were used in the assignment of carbon spectra. One dimensional nuclear Overhauser spectroscopy was conducted using the 1D-NOESY pulse sequence. Two dimensional NMR experiments were recorded on a Varian Mercury 300 spectrometer. Short range carbon–hydrogen correlation experiments were conducted *via* indirect detection using the gHMQC pulse sequence. Where THP protecting groups have been used, integrations relate to individual diastereomers; where peaks are superimposed, integrations indicate the sum of both diastereomers. Thus, a single methyl peak integrates to 6 H. Assignment of the anomeric protons of the diastereomers has been made where possible, and designated as THP-H1 and THP-H1′ in the proton NMR; similarly, where possible, the anomeric carbon is assigned as THP-C1 and THP-C1′ in ^{13}C-NMR spectra. The balance of protons associated with the THP group have been designated THP where possible. Low resolution (LRMS) EI mass spectra (70 eV) were recorded on a Fisons VG autospec double focusing mass spectrometer, and ESI mass spectra were recorded on a Micromass single quadrupole mass spectrometer. High resolution (HRMS) EI mass spectra were recorded on a Fisons VG autospec double focusing mass spectrometer. The molecular ion (M^+), if present, significant high mass ions and the more intense low mass ions are reported. Flash chromatography was conducted on Merck Kieselgel 60 as the adsorbent. High performance liquid chromatography (HPLC) was carried out using Waters 510 HPLC pumps, and a Waters Lambda-Max 481 ultra violet detector set at either 210 or 254 nm. Alltima C18 columns were supplied by Altech.

ent-10β-Hydroxy-3,4-seco-20-nor-4β-gibberell-16-ene-3,7,19-trioic acid 7-methyl ester 19,10-lactone (7) plus 4-epimer

To a stirred solution of **6** (2.5 g, 7.3 mmol) in THF (56 mL) at 0 °C was added a cooled solution of 1.0 M NaOH (14 mL, 14.6 mmol). After 8 min the reaction was quenched with 1.0 M HCl (20 mL), diluted with EtOAc (100 mL) and washed with water until pH 4.5. The aqueous layers were extracted with EtOAc (100 mL) and the combined organic layers extracted with saturated aqueous $NaHCO_3$ (2 × 100 mL). The basic aqueous extracts were then neutralised with 1.0 M HCl and extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with water (200 mL), brine (200 mL) and dried (Na_2SO_4). The solvent was removed *in vacuo* to afford **7** (2.3 g, 87%) as a 9 : 1 (*endo* : *exo*) ratio of C-4 epimers. **7**: mp 140–145 °C (from EtOAc–petroleum spirits bp 60–80 °C); found: C, 66.2; H, 6.9. $C_{20}H_{26}O_6$ requires C, 66.3; H, 7.2%; ν_{max} (thin film)/cm^{-1} 3200, 1767, 1728, 1437, 1310, 1170; δ_H (300 MHz; $CDCl_3$) 1.22 (3 H, d, *J* 7.0, H-18), 1.40–1.60 (3 H, m), 1.65–1.80 (3 H, m), 1.95–2.15 (3 H, m), 2.17–2.32 (1 H, m, H-9), 2.40 (1 H, dt, $J_{15,17}$ 2.9, J_{gem} 15.8, H-15), 2.45–2.6 (2 H, m), 2.68 (1 H, br s, H-13), 2.76 (1 H, d, *J* 2.5, H-6), 2.98 (1 H, dq, $J_{4,18}$ 7.1, $J_{4,5}$ 10.8, H-4), 3.07 (1 H, dd, $J_{5,6}$ 2.6, $J_{5,6}$ 10.8, H-5), 3.68 (3 H, s, $-CO_2CH_3$), 4.90 (2 H, br s, H-17); δ_C (75 MHz; $CDCl_3$) 12.3 (C-18), 17.4 (C-11), 29.5 (C-1 or C-2), 32.3 (C-12), 32.8 (C-1 or C-2), 38.6 (C-4), 41.0 (C-14), 41.6 (C-13), 42.6 (C-15), 49.6 (C-9), 50.7 and 51.3 (C-5 and C-6), 52.5 ($-CO_2\mathit{C}H_3$), 53.0 (C-8), 96.0 (C-10), 107.3 (C-17), 152.9 (C-16), 175.4 (C-7), 178.9 (C-19), 179.8 (C-3); *m/z* (EI) 362.1728 (M^+ $C_{20}H_{26}O_6$ requires 362.1729), 344 (44%), 330 (65), 316 (100), 302 (84), 274 (83), 257 (74), 229 (65), 201 (49), 173 (50), 105 (58), 91 (75).

epi-**7**: ν_{max} (thin film)/cm^{-1} 3160, 3040, 1762, 1721, 1435, 1200; δ_H (300 MHz; $CDCl_3$) 1.41 (3 H, d, *J* 7.4, H-18), 1.45–1.80 (6 H, m), 1.98 (1 H, d, *J* 15.6, H-15), 2.01–2.15 (3 H, m), 2.20–2.60 (7 H, m), 2.70 (1 H, br s, H-13), 3.69 (3 H, s, $-CO_2CH_3$), 4.93 (2 H, br s, H-17); δ_C (75 MHz; $CDCl_3$) 16.7 (C-11), 18.0 (C-18), 29.0 (C-1 or C-2), 31.8 (C-12), 34.0 (C-1 or C-2), 40.9 (C-14), 41.2 (C-13), 41.6 (C-15), 44.6 (C-4), 49.1 (C-6), 51.8 ($-CO_2\mathit{C}H_3$), 53.0 (C-9), 53.2 (C-8), 58.9 (C-5), 95.5 (C-10), 106.6 (C-17), 151.3 (C-16), 174.6 (C-7), 177.3 (C-19), 179.5 (C-3); *m/z* (EI) 362.1729 (M^+ $C_{20}H_{26}O_6$ requires 362.1729), 344 (17%), 330 (29), 316 (100), 303 (87), 288 (57), 274 (59), 256 (47), 242 (21), 229 (54), 211 (21), 201 (29).

ent-3,10β-Dihydroxy-3,4-seco-20-nor-4β-gibberell-16-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (8)

Et$_3$N (770 μL, 5.6 mmol) and ethyl chloroformate (530 μL, 5.6 mmol) were added dropwise to a stirred solution of **7** (1 g, 2.8 mmol) in THF (30 mL) at 0 °C. The solution was stirred at 0 °C for 30 min, then at 20 °C for 4 h, after which NaBH$_4$ (210 mg, 5.6 mmol) was added as an ethanolic suspension (10 mL) at 0 °C. After a further 2 h, 1.0 M HCl (5 mL) and water (5 mL) were added and the solution stirred for 30 min. The reaction mixture was diluted with EtOAc (100 mL) and washed with 1.0 M HCl (2 × 50 mL) and the combined aqueous layers extracted with EtOAc (100 mL). The combined organic extracts were washed with aqueous NaHCO$_3$ (150 mL), the basic aqueous layers extracted with EtOAc (100 mL) and the combined organic layers washed with brine (100 mL) and dried (Na$_2$SO$_4$). Concentration *in vacuo* and column chromatography on silica (15% EtOAc and 85% petroleum spirits bp 60–80 °C, increasing to 75% EtOAc) afforded **8** (537 mg, 55% conversion, 70% yield) as a colourless solid mp 93–95 °C (from EtOAc–petroleum spirits bp 60–80 °C); found: C, 68.8; H, 8.0 C$_{20}$H$_{28}$O$_5$ requires C, 68.9; H, 8.1%; ν_{max} (thin film)/cm^{-1} 3444, 2934, 1762, 1729, 1659, 1367, 1268, 1193, 1170, 1059; δ_H (300 MHz; CDCl$_3$) 1.22 (3 H, d, *J* 7.4, H-18), 1.47–2.10 (15 H, m), 2.39 (1 H, dt, $J_{15,17}$ 2.8, J_{gem} 15.7, H-15), 2.67 (1 H, br s, H-13), 2.76 (1 H, d, *J* 2.7, H-6), 2.99 (1 H, dq, $J_{4,18}$ 7.2, $J_{4,5}$ 10.7, H-4), 3.09 (1 H, dd, $J_{5,6}$ 3.0, $J_{5,4}$ 10.7, H-5), 3.68 (2 H, t, *J* 5.8, H-3), 3.69 (3 H, s, –CO$_2$CH$_3$), 4.92 (2 H, d, *J* 3.2, H-17); δ_C (75 MHz; CDCl$_3$) 11.7 (C-18), 16.7 (C-11), 27.0 (C-1 or C-2), 31.6 (C-12), 33.7 (C-1 or C-2), 38.2 (C-4), 40.4 (C-15), 40.9 (C-13), 42.0 (C-14), 49.1 (C-9), 50.3 and 50.6 (C-5 and C-6), 51.7 (–CO$_2$*C*H$_3$), 52.3 (C-18), 62.5 (C-3), 96.2 (C-10), 106.5 (C-17), 152.5 (C-16), 174.9 (C-7), 179.4 (C-19); *m*/*z* (EI) 348.1937 (M$^+$ C$_{20}$H$_{28}$O$_5$ requires 348.1937), 330 (5%), 316 (81), 289 (79), 260 (100), 244 (66), 215 (36), 201 (63), 173 (59), 91 (61).

ent-3-*tert*-Butyldimethylsilyloxy-10β-hydroxy-3,4-seco-20-nor-4β-gibberell-16-ene-7,19-dioic acid 7-methyl ester 19,10-lactone

To a stirred solution of **8** (2.0 g, 5.7 mmol) and imidazole (78 mg, 1.14 mmol) in DMF (16 mL) at 0 °C was added Et$_3$N (1.6 mL, 11.4 mmol) and TBDMSCl (1.7 g, 11.4 mmol) in DMF (10 mL). The solution was allowed to warm to rt and stir for 2.5 h. The reaction mixture was diluted with EtOAc (100 mL) and washed with water (3 × 200 mL). The combined aqueous layers were extracted with EtOAc (2 × 100 mL), and the combined organic layers washed with brine (100 mL) and dried (Na$_2$SO$_4$). Concentration *in vacuo* and column chromatography on silica (5% EtOAc and 95% petroleum spirits bp 60–80 °C) afforded the title compound (2.63 g, 100%) as a colourless oil. ν_{max} (thin film)/cm^{-1} 2920, 2850, 1765, 1730, 1655, 1470, 1360, 1310, 1250, 1200, 1155, 1100, 955, 880, 775; δ_H (300 MHz; CDCl$_3$) 0.03 (6 H, s, –SiCH$_3$), 0.88 (9 H, s, –Si*t*-Bu), 1.21 (3 H, s, H-18), 1.25–1.35 (12 H, m), 2.37 (1 H, dt, $J_{15,17}$ 2.8, J_{gem} 15.8, H-15), 2.99 (1 H, br s, H-13), 2.75 (1 H, d, *J* 2.9, H-6), 2.96 (1 H, dq, $J_{4,18}$ 7.3, $J_{4,5}$ 10.4, H-4), 3.08 (1 H, dd, $J_{5,6}$ 3.0, $J_{5,4}$ 10.5, H-5), 3.61 (2 H, t, *J* 6.2, H-3), 3.68 (3 H, s, –CO$_2$CH$_3$), 4.91 (2 H, d, *J* 5.3, H-17); δ_C (75 MHz; CDCl$_3$) −5.6 (–SiCH$_3$), 11.5 (C-18), 16.5 (C-11), 18.0 (–Si–*C*(CH$_3$)$_3$), 25.6 (–Si–C(*C*H$_3$)$_3$), 27.0 (C-1 or C-2), 31.5 (C-12), 33.4 (C-1 or C-2), 38.0 (C-4), 40.2 (C-15), 40.8 (C-13), 41.8 (C-14), 48.9 (C-9), 50.1 and 50.5 (C-5 and C-6), 51.4 (–CO$_2$*C*H$_3$), 52.1 (C-8), 62.5 (C-3), 96.0 (C-10), 106.2 (C-17), 152.4 (C-16), 174.5 (C-19), 179.0 (C-7); *m*/*z* (EI) 405.2094 (M$^+$−57 C$_{22}$H$_{33}$O$_5$Si requires 405.2097), 405 (86%), 373 (100), 347 (51), 317 (50), 303 (39), 257 (18), 255 (48), 197 (30), 171 (13), 131 (16), 75 (44).

ent-4α-Bromo-3-*tert*-butyldimethylsilyloxy-10β-hydroxy-3,4-seco-20-norgibberell-16-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (9)

LDA (0.5 M) in THF (1.96 mL, 0.98 mmol) was added dropwise to a stirred solution of the TBS ether prepared above (320 mg, 0.65 mmol) in THF (3.5 mL) at −78 °C, after 25 min CBr$_4$ (541 mg, 1.63 mmol) in THF (1.5 mL) was added dropwise over 5 min. After a further 40 min the reaction was quenched with saturated aqueous NH$_4$Cl (2.0 mL) at −78 °C and allowed to warm to rt. The brown reaction mixture was diluted with EtOAc (50 mL) and washed with water (2 × 20 mL). The combined aqueous layers were extracted with EtOAc (2 × 20 mL), the combined organic extracts washed with brine (50 mL) and dried (Na$_2$SO$_4$). Concentration *in vacuo* and column chromatography on silica (4% EtOAc and 96% petroleum spirits bp 60–80 °C) afforded the title compound (348 mg, 99%) as a pale brown oil. ν_{max} (thin film)/cm^{-1} 3567, 3336, 2952, 2930, 2858, 1775, 1734, 1656, 1455, 1427, 1381, 1360, 1254, 1169, 1102, 1072, 1049, 938, 836; δ_H (300 MHz; CDCl$_3$) 0.03 (6 H, s, –SiCH$_3$), 0.87 (9 H, s, –Si*t*-Bu), 1.3–1.8 (7 H, m), 1.93 (3 H, s, H-18), 1.98 (1 H, d, *J* 15.9, H-15), 2.10–2.22 (4 H, m), 2.41 (1 H, dt, $J_{15,17}$ 2.0, J_{gem} 15.9, H-15), 2.66 (1 H, br s, H-13), 2.79 (1 H, d, *J* 2.3, H-6), 3.58 (1 H, d, *J* 2.3, H-5), 3.63 (2 H, t, *J* 5.9, H-3), 3.69 (3 H, s, –CO$_2$CH$_3$), 4.90 (2 H, s, H-17); δ_C (75 MHz; CDCl$_3$) −4.7 (–SiCH$_3$), 17.0 (C-11), 18.8 (–Si–*C*(CH$_3$)$_3$), 26.2 (C-18), 26.5 (–Si–C(*C*H$_3$)$_3$), 28.5 (C-1 or C-2), 32.2 (C-12), 33.7 (C-1 or C-2), 41.3 (C-15), 41.8 (C-13), 42.2 (C-14), 48.4 (C-9), 52.5 (–CO$_2$*C*H$_3$), 52.8 (C-8), 53.6 (C-6), 56.2 (C-4), 59.4 (C-5), 63.3 (C-3), 97.8 (C-10), 107.3 (C-17), 152.1 (C-16), 174.2 (C-19), 175.2 (C-7); *m*/*z* (EI) 485.1178 (M$^+$−57 $C_{22}H_{32}O_5{}^{81}BrSi$ requires 485.1182), 453/451 (30%), 405/403 (42), 371 (100), 343 (49), 317 (24), 283 (18), 257 (20), 225 (37), 197 (31), 171/169 (19), 75 (55).

ent-3,10β-Dihydroxy-3,4-seco-20-nor-4β-gibberell-4 (18), 16-diene-7,19-dioic acid 7-methyl ester 19,10-lactone (10)

TBAF (1.0 M) in THF (278 μL, 279 μmol) was added dropwise to a stirred solution of the bromide prepared above (50 mg, 93 μmol) in THF (1.0 mL) at 0 °C. The solution was allowed to warm to rt and after 4 h was diluted with EtOAc (15 mL) and washed with water (2 × 15 mL). The combined aqueous layers were extracted with EtOAc (20 mL), and the combined organic extracts washed with brine (25 mL) and dried (Na$_2$SO$_4$). Concentration *in vacuo* and column chromatography on silica (40% EtOAc and 60% petroleum spirits bp 60–80 °C) afforded **10** (20 mg, 62%) as a pale yellow oil. ν_{max} (thin film)/cm^{-1} 3442, 3067, 2933, 2861, 1758, 1732, 1659, 1437, 1403, 1353, 1246, 1196, 1127, 1095, 1060, 971, 818, 780; δ_H (300 MHz; CDCl$_3$) 1.35–1.80 (16 H, m), 1.95 (1 H, d, J_{gem} 16.9, H-14), 2.00–2.12 (2 H, m), 2.46 (1 H, dt, $J_{15,17}$ 3.0, J_{gem} 15.9, H-15), 2.60 (1 H, s, H-6), 2.66 (1 H, br s, H-13), 3.50 (1 H, s, H-5), 3.65 (2 H, td, *J* 1.8, 6.4, H-3), 3.71 (3 H, s, –CO$_2$CH$_3$), 4.91 (2 H, s, H-17), 5.70 (1 H, d, *J* 2.3, H-18), 6.29 (1 H, d, *J* 2.6, H′-18); δ_C (75 MHz; CDCl$_3$) 16.5 (C-11), 26.7 (C-1), 31.6 (C-12), 34.6 (C-2), 41.0 (C-14), 41.2 (C-13), 41.3 (C-15), 49.3 (C-9), 49.7 (C-6), 51.8 (–CO$_2$*C*H$_3$), 53.1 (C-8), 60.2 (C-5), 62.3 (C-3), 95.2 (C-10), 106.4 (C-17), 123.6 (C-18), 140.7 (C-4), 151.6 (C-16), 170.3 (C-19), 174.2 (C-7); *m*/*z* (EI) 346.1784 (M$^+$ $C_{20}H_{26}O_5$ requires 346.1780), 328 (37%), 314 (69), 300 (41), 296 (46), 286 (100), 268 (27), 255 (16), 241 (25), 227 (63), 199 (39), 171 (29), 129 (27), 105 (22), 91 (48), 79(25).

ent-10β-Hydroxy-3-oxo-3,4-seco-20-4β-norgibberell-4 (18), 16-diene-7,19-dioic acid 7-methyl ester 19,10-lactone (11)

To a stirred solution of **10** (1.5 g, 4.4 mmol) in CH_2Cl_2 (44 mL) was added Dess–Martin periodinane (2.8 g, 6.6 mmol), after 20 min the solvent was removed *in vacuo* and the resulting solid subjected to column chromatography on silica (40% EtOAc and 60% petroleum spirits bp 60–80 °C) to yield **11** (1.34 g, 89%) as a pale yellow oil. ν_{max} (thin film)/cm^{-1} 3330, 2932, 1761, 1729, 1658, 1438, 1402, 1353, 1289, 1273, 1197, 1168, 1095, 1073, 970, 889; δ_H (300 MHz; $CDCl_3$) 1.38 (2 H, br s), 1.50–1.80 (4 H), 1.93 (1 H, d, J_{gem} 17.5, H-14), 1.95–2.10 (2 H, m), 2.27 (1 H, m, H-9), 2.45 (1 H, d, J_{gem} 15.6, H-15), 2.58 (1 H, s, H-6), 2.63 (1 H, br s, H-13), 3.42 (1 H, s, H-5), 3.68 (3 H, s, –CO$_2$CH$_3$), 5.70 (2 H, d, *J* 1.7, H-17), 6.29 (1 H, d, *J* 2.7, H-18), 7.25 (1 H, d, *J* 2.6, H′-18), 9.73 (1 H, s, H-3); δ_C (75 MHz; $CDCl_3$) 16.2 (C-11), 30.1 (C-1), 31.3 (C-12), 37.9 (C-2), 40.6 (C-15), 40.8 (C-13), 41.0 (C-14), 48.7 (C-9), 49.4 (C-6), 51.5 (–CO$_2$*C*H$_3$), 52.8 (C-8), 59.8 (C-5), 93.8 (C-10), 106.2 (C-17), 123.8 (C-18), 139.9 (C-4), 151.0 (C-16), 169.5 (C-19), 173.7 (C-7), 200.3 (C-3); *m*/*z* (EI) 344.1630 (M$^+$ $C_{20}H_{24}O_5$ requires 344.1624), 326 (63%), 312 (100), 298 (57), 284 (84), 268 (68), 240 (75), 227 (59), 199 (52), 129 (53), 91 (68).

ent-18-Allyloxy-3α,10β-dihydroxy-20-norgibberell-16-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (12)

To a stirred solution of **11** (500 mg, 1.45 mmol) in allyl alcohol (15 mL) was added K_2CO_3 (1.0 g, 7.25 mmol). After 80 min, 1.0 M HCl was carefully added, the solution diluted with EtOAc (50 mL) and washed with water (2 × 20 mL). The combined aqueous layers were extracted into EtOAc (2 × 50 mL), and the combined organic extracts washed with brine (50 mL) and dried (Na_2SO_4). Concentration *in vacuo* and column chromatography on silica (15% EtOAc and 85% petroleum spirits bp 60–80 °C, increasing to 60% EtOAc) afforded **12** (192 mg, 33%) and then *epi*-**12** (135 mg, 23%).

12: mp 125–126 °C (from EtOAc–petroleum 60–80 °C); found C, 68.3; H, 7.5 $C_{23}H_{30}O_6$ requires C, 68.6; H, 7.5%; ν_{max} (thin film)/cm^{-1} 3495, 3068, 2944, 1773, 1736, 1656, 1436, 1384, 1347, 1278, 1245, 1197, 1170, 1098, 1070, 1020, 99, 884; δ_H (300 MHz; $CDCl_3$) 1.30–2.10 (11 H, m), 2.17 (1 H, d, J_{gem} 15.5, H-15), 2.62 (1 H, t, *J* 6.5, H-13), 2.76 (1 H, d, $J_{6,5}$ 10.5, H-6), 3.47 (1 H, d, $J_{5,6}$ 10.6, H-5), 3.51 (1 H, d, J_{gem} 9.9, H-18), 3.67 (3 H, s, –CO$_2$CH$_3$), 3.88 (1 H, d, J_{gem} 9.8, H′-18), 3.90 (1 H, m, H-1′), 3.95 (1 H, dd, $J_{1',2'}$ 5.5, J_{gem} 10.0, H-1′), 4.15 (1 H, d, *J* 2.6, H-3), 4.85 (1 H, s, H-17), 4.96 (1 H, s, H′-17), 5.20 (1 H, d, J_{cis} 4.1, H-3′), 5.25 (1 H, d, J_{trans} 11.7, H-3′), 5.80 (1 H, m, H-2′); δ_C (75 MHz; $CDCl_3$) 16.0 (C-11), 27.1 (C-1 and C-2), 31.2 (C-12), 37.7 (C-14), 38.9 (C-13), 44.7 (C-15), 49.8 (C-9), 51.3 (C-6), 51.7 (–CO$_2$*C*H$_3$), 51.8 (C-8), 53.2 (C-5), 57.5 (C-4), 70.5 (C-3), 71.4 and 72.7 (C-18 and C-1′), 95.8 (C-10), 107.2 (C-17), 118.2 (C-3′), 133.1 (C-2′), 156.5 (C-16), 172.8 (C-19), 175.0 (C-7); *m*/*z* (EI) 402.2046 (M$^+$ $C_{23}H_{30}O_6$ requires 402.2042), 384 (34%), 370 (100), 353 (11), 342 (32), 326 (34), 312 (27), 298 (23), 284 (47), 268 (30), 254 (44), 240 (39), 223 (21), 195 (14), 141 (66), 129 (21), 105 (15), 91 (33), 79 (18).

epi-**12**: mp 105 °C (from EtOAc–petroleum 60–80 °C); ν_{max} (thin film)/cm^{-1} 3449, 3070, 2944, 2865, 1773, 1734, 1656, 1436, 1384, 1343, 1271, 1170, 1134, 1099, 1076, 1049, 973, 888; δ_H (300 MHz; $CDCl_3$) 1.30–1.75 (6 H, m), 1.89 (1 H, dt, $J_{15,17}$ 2.8, J_{gem} 15.4, H-15), 1.95–2.25 (6 H, m), 2.60 (1 H, t, *J* 6.6, H-13), 2.65 (1 H, d, $J_{6,5}$ 10.2, H-6), 2.93 (1 H, d, $J_{5,6}$ 10.0, H-5), 3.59 (1 H, d, J_{gem} 9.9, H-18), 3.65 (3 H, s, –CO$_2$CH$_3$), 3.83 (1 H, d, J_{gem} 10.1, H′-18), 3.88 (2 H, m, H-1′), 3.96 (1 H, m, H-3), 4.83 (1 H, s, H-17), 4.94 (1 H, s, H′-17), 5.14 (1 H, dd, $J_{gem'}$ 1.5, J_{cis} 10.4, H-3′), 5.22 (1 H, dd, J_{gem} 1.6, J_{trans} 17.3, H-3′), 5.79 (1 H, m, H-2′); δ_C (75 MHz; $CDCl_3$) 16.0 (C-11), 29.0 and 29.9 (C-1 and C-2), 31.3 (C-12), 37.3 (C-14), 38.8 (C-13), 44.5 (C-15), 51.4 (C-9), 51.4 (–CO$_2$*C*H$_3$), 52.4 (C-8), 52.7 (C-6), 55.0 (C-5), 58.2 (C-4), 66.4 (C-1′), 69.8 (C-3), 72.4 (C-18), 93.8 (C-10), 107.2 (C-17), 117.2 (C-3′), 134.0 (C-2′), 152.4 (C-16), 173.0 (C-19), 175.1 (C-17); *m*/*z* (EI) 402.2038 (M$^+$ $C_{23}H_{30}O_6$ requires 402.2042), 384 (22%), 370 (100), 352 (44), 342 (37), 326 (55), 312 (67), 298 (54), 284 (60), 268 (68), 256 (44), 240 (57), 228 (36), 181 (26), 169 (34), 129 (47), 105 (36), 91 (79), 79 (43).

ent-3α,10β,18-Trihydroxy-20-norgibberell-16-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (13)

A stirred, degassed solution of **12** (217 mg, 0.54 mmol), RhCl(PPh$_3$)$_3$ (100 mg, 0.11 mmol) and DABCO (30 mg, 0.27 mmol) in 10% aqueous EtOH (5.5 mL), was heated at 75 °C for 24 h after which RhCl(PPh$_3$)$_3$ (100 mg, 0.11 mmol) and DABCO (30 mg, 0.27 mmol) were added. The solution was heated at 75 °C for a further 24 h, allowed to cool, 1.0 M HCl (2.0 mL) added and stirring continued for 30 min. The solution was diluted with EtOAc (20 mL) and washed with water (2 × 25 mL). The aqueous layers were extracted into EtOAc (3 × 20 mL), and the combined organic extracts washed with brine (30 mL) and dried (Na_2SO_4). Concentration *in vacuo* and column chromatography on silica (10% CH, 40% EtOAc and 50% petroleum spirits bp 60–80 °C) followed by recrystallisation from CH_2Cl_2 and petroleum spirits bp 60–80 °C gave **13** (55 mg, 37% based on 77% conversion) as a colourless solid mp 166–167 °C (from EtOAc–petroleum 60–80 °C); found: C, 66.0; H, 7.4 $C_{20}H_{26}O_6$ requires C, 66.3; H, 7.2%; ν_{max} (thin film)/cm^{-1} 3441, 3065, 2944, 2880, 1766, 1735, 1658, 1438, 1382, 1267, 1199, 1019, 888; δ_H (300 MHz; $CDCl_3$) 1.30–2.15 (13 H, m), 2.63 (1 H, t, *J* 7.1, H-13), 2.86 (1 H, d, $J_{6,5}$ 11.4, H-6), 3.35 (1 H, d, $J_{5,6}$ 11.4, H-5), 3.66 (1 H, d, J_{gem} 12.6, H-18), 3.76 (3 H, s, –CO$_2$CH$_3$), 3.99 (1 H, d, 12.7, H′-18), 4.28 (1 H, d, *J* 2.4, H-3), 4.89 (1 H, s, H-17), 5.02 (1 H, s, H′-17). δ_C (75 MHz; $CDCl_3$) 16.1 (C-11), 27.2 and 27.3 (C-1 and C-2), 31.4 (C-12), 36.1 (C-14), 38.2 (C-13), 43.7 (C-15), 48.1 (C-9), 50.6 (C-6), 50.9 (C-8), 52.4 (–CO$_2$*C*H$_3$), 53.5 (C-5), 58.0 (C-4), 64.0 (C-18), 70.0 (C-3), 94.5 (C-10), 107.9 (C-17), 156.7 (C-16), 174.8 (C-19), 175.3 (C-7); *m*/*z* (EI) 362.1729 (M$^+$ $C_{20}H_{26}O_6$ requires 362.1729), 344 (18%), 330 (100), 312 (92), 284 (60), 266 (60), 240 (60), 195 (20), 155 (30), 129 (43), 115 (34), 91 (78), 79 (47).

ent-3α,10β-Dihydroxy-16-oxo-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone

Through a stirred solution of GA$_4$ methyl ester (26.22 g, 75.8 mmol) in EtOH (700 mL) at −10 °C was bubbled ozone. After

3 h, the ozone flow was stopped and oxygen bubbled through, then after 15 min the reaction was allowed to warm to 0 °C and water (90 mL), acetic acid (45 mL) and zinc powder added. The mixture was allowed to warm to rt and stirred for 16 h, then filtered and concentrated *in vacuo* almost to dryness. The resulting residue was taken up in water (500 mL) and extracted with CH_2Cl_2 (2 × 600 mL), then the combined organic extracts were washed with water (4 × 500 mL), brine (200 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (75% EtOAc and 25% hexane) afforded the title compound (23.7 g, 90%) as a white powder mp 203–204 °C (from EtOAc–hexane); (found: C, 65.2; H, 7.0 $C_{19}H_{24}O_6$ requires C, 65.5; H, 6.9). ν_{max} (thin film)/cm^{-1} 3507, 2948, 2877, 1771, 1737, 1436, 1376, 1281, 1195, 1171, 1016, 922; δ_H (300 MHz; $CDCl_3$) 1.15 (3 H, s, H-18), 1.51–2.20 (13 H, m), 2.43 (1 H, m, H-13), 2.71 (1 H, d, *J* 10.9, H-6), 3.21 (1 H, d, *J* 10.7, H-5), 3.71 (3 H, s, $-CO_2CH_3$), 3.84 (1 H, t, *J* 2.4, H-3); δ_C (75 MHz; $CDCl_3$) 14.7(C-18), 16.8 (C-11), 25.0 (C-12), 27.1 (C-1), 28.0 (C-2), 34.5 (C-14), 44.7 (C-13), 49.8 (C-8), 50.4 (C-15), 51.0 (C-5), 52.3 ($-CO_2CH_3$), 52.6 (C-6), 53.9 (C-9), 54.6 (C-4), 69.9 (C-3), 93.7 (C-10), 172.3 (C-7), 177.8 (C-19), 220.2 (C-16); *m/z* (EI) 348.1573 (M^+ $C_{19}H_{24}O_6$ requires 348.1573), 762 (8%), 718 (7), 697 (11), 696 (22), 444 (9), 428 (10), 426 (38), 408 (59), 394 (53), 380 (22), 364 (52), 348 (100), 326 (20), 316 (12), 282 (5), 242 (13).

ent-10β-Hydroxy-3,16-dioxo-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (14)

To a stirred solution of the ketone prepared above (1.91 g, 5.50 mmol) in CH_2Cl_2 (40 mL) was added Dess–Martin periodinane (3.62 g, 8.24 mmol). After 1 h, saturated $NaHCO_3$ (20 mL) and 1.0 M $Na_2S_2O_3$ (20 mL) were added, and once both layers had turned clear the reaction was diluted with EtOAc (120 mL) and washed with water (3 × 75 mL). The combined aqueous extracts were back-extracted with EtOAc (2 × 50 mL), then the combined organic layers washed with brine (100 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (25% EtOAc and 75% hexane, increasing to 67% EtOAc) afforded **3** (1.88 g, 99%) as a white powder mp 203–204 °C (from EtOAc–hexane); (found: C, 65.6; H, 6.8 $C_{19}H_{22}O_6$ requires C, 65.9; H, 6.4). ν_{max} (thin film)/cm^{-1} 2946, 1779, 1735, 1448, 1382, 1270, 1169, 1036, 958, 931, 891; δ_H (300 MHz; $CDCl_3$) 1.19 (3 H, s, H-18), 1.66–2.26 (10 H, m), 2.45–2.66 (4 H, m), 2.85 (1 H, d, *J* 10.1, H-6), 3.11(1 H, d, *J* 10.0, H-5), 3.73 (3 H, s, $-CO_2CH_3$); δ_C (75 MHz; $CDCl_3$) 10.4 (C-18), 16.9 (C-11), 24.9 (C-12), 30.7 (C-1), 34.6 (C-14), 34.9 (C-2), 44.5 (C-13), 50.2 (C-15), 51.3 (C-8), 52.6 ($-CO_2CH_3$), 52.8 (C-6), 53.5 (C-9), 56.8 (C-5), 63.1 (C-4), 92.4 (C-10), 171.4 (C-19), 173.4 (C-7), 199.5 (C-3), 219.0 (C-16); *m/z* (EI) 346.1420 (M^+ $C_{19}H_{22}O_6$ requires 346.1416), 318 (100%), 301 (8), 286 (25), 274 (21), 258 (19), 242 (22), 213 (12), 199 (11), 129 (13), 115 (14), 105 (13), 91 (29), 77 (20), 55 (22).

ent-10β-Hydroxy-16-oxo-3,4-seco-17,20-dinor-4β-gibberellane-3,7,19-trioic acid 7-methyl ester 19,10-lactone

To a stirred solution of **14** (1.00 g, 2.90 mmol) in THF (30 mL) at 0 °C was added a cooled solution of 1.0 M NaOH (5.80 mL, 5.80 mmol). After 2 min 45 s the reaction was quenched with 1.0 M HCl (8.36 mL), diluted with EtOAc (40 mL) and washed with water (6 × 50 mL). The aqueous layers were back-extracted with EtOAc (2 × 100 mL) and the combined organic layers extracted with saturated aqueous $NaHCO_3$ (2 × 100 mL). The basic aqueous extracts were then acidified with 1.0 M HCl and extracted with EtOAc (3 × 125 mL). The combined organic extracts were washed with water (3 × 75 mL), brine (200 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to afford the title compound (1.00 g, 95%) as an 18 : 1 (*endo* : *exo*) ratio of C-4 epimers. ν_{max} (thin film)/cm^{-1} 2947, 1764, 1735, 1437, 1309, 1235, 1176, 1161, 959, 754; δ_H (300 MHz; $CDCl_3$) 1.24 (d, *J* 7.2, 3 H, H-18), 1.66–2.50 (14 H, m), 2.86 (1 H, d, *J* 2.8, H-6), 3.06 (1 H, m, H-4), 3.15 (1 H, dd, *J* 2.8 and 10.8, H-5), 3.68 (3 H, s, $-CO_2CH_3$); δ_C (75 MHz; $CDCl_3$) 11.8 (C-18), 17.3 (C-11), 28.3 (C-12), 28.9 and 32.1 (C-1 and C-2), 38.1 (C-4), 38.2 (C-14), 46.2 (C-13), 48.8 (C-15), 49.1 (C-9), 50.0 (C-5 or C-6), 50.7 (C-8), 50.8 (C-5 or C-6), 52.2 ($-CO_2CH_3$), 94.7 (C-10), 173.8 (C-7), 177.6 (C-19), 178.5 (C-3), 218.9 (C-16); *m/z* (EI) 364.1526 (M^+ $C_{19}H_{24}O_7$ requires 364.1522), (LRMS ESI+) 730 (45%), 729 (100), 715 (10), 391 (6), 366 (8), 365 (38), 347 (40), 333 (11).

ent-3,10β,16α-Trihydroxy-3,4-seco-17,20-dinor-4β-gibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (15)

To a stirred solution of seco-acid prepared above (1.70 g, 4.67 mmol) in THF (30 mL) at −18 °C was added dropwise 1.7 M borane–dimethylsulfide complex in THF (3.66 mL, 6.23 mmol). The reaction mixture was allowed to slowly warm to rt, then after 15.5 h cooled to 0 °C and water (9.6 mL) then K_2CO_3 (3.86 g) added. The organic phase was separated, and the aqueous phase extracted with 20% 2-butanol in EtOAc (4 × 25 mL). The combined organic extracts were washed with brine (50 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to afford **15** (1.39 g, 85%) ν_{max} (thin film)/cm^{-1} 3369, 2928, 1753, 1730, 1436, 1307, 1246, 1178, 1044, 964; δ_H (300 MHz; $CDCl_3$) 1.16 (3 H, d, *J* 6.9, H-18), 1.21–2.22 (14 H, m), 2.70 (1 H, d, *J* 1.6, H-6), 3.09–3.15 (2 H, m, H-4 and H-5), 3.59 (2 H, t, *J* 6.3, H-3), 3.67 (3 H, s, $-CO_2CH_3$), 4.34 (1 H, m, H-16); δ_C (75 MHz; $CDCl_3$) 12.1 (C-18), 17.7 (C-11), 24.9 (C-12), 28.2 and 34.9 (C-1 and C-2), 39.6 (C-4), 39.9 (C-14), 40.1 (C-13), 43.9 (C-15), 50.7 (C-9), 52.1 and 52.6 (C-5 and C-6), 52.9 ($-CO_2CH_3$), 53.0 (C-8), 62.8 (C-3), 72.7 (C-16), 98.0 (C-10), 176.1 (C-7), 181.7 (C-19); *m/z* (EI) 352.1883 (M^+ $C_{19}H_{28}O_6$ requires 352.1886), (LRMS ESI+) 728 (47%), 727 (93), 699 (21), 428 (6), 396 (13), 376 (21), 375 (100), 353 (19), 347 (10).

ent-3,16α-Bis-*tert*-butyldimethylsilyloxy-10β-hydroxy-3,4-seco-17,20-dinor-4β-gibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (16)

To a stirred solution of **15** (0.82 g, 2.3 mmol) and imidazole (32 mg, 0.47 mmol) in DMF (7 mL) at 0 °C was added Et_3N (1.3 mL, 9.36 mmol) and TBDMSCl (1.41 g, 9.36 mmol) in DMF (7 mL). The solution was allowed to warm to rt and stirred for 6 h, then a second addition of Et_3N (325 μL, 2.34 mmol) and TBDMSCl (353 mg, 2.34 mmol) in DMF (2 mL) was made. After 1 h, the reaction mixture was diluted with EtOAc (25 mL) and washed with water (4 × 15 mL). The combined aqueous layers were extracted with EtOAc (2 × 15 mL), and the combined organic layers washed with brine (40 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (5% EtOAc and 95% hexane) afforded **16** (2.63 g, 100%) as a pale yellow oil. ν_{max} (thin film)/cm^{-1} 2952, 2930, 2886, 2857, 1768, 1733, 1471, 1361, 1309, 1254, 1192, 1162, 1092, 966, 892, 836, 775; δ_H (300 MHz; CDCl$_3$) 0.01 (6 H, s, –SiCH$_3$), 0.04 (6 H, s, –SiCH$_3$), 0.87 (9 H, s, –Si*t*-Bu), 0.88 (9 H, s, –Si*t*-Bu), 1.19 (3 H, d, *J* 7.0, H-18), 1.36–2.15 (14H, m), 2.62 (1 H, d, *J* 2.8, H-6), 2.96 (1H, m, H-4), 3.04 (1 H, dd, $J_{5,6}$ 2.7, $J_{5,4}$ 10.6, H-5), 3.63 (2 H, dt, *J* 6.0, 1.5, H-3), 3.66 (3 H, s, –CO$_2$CH$_3$), 4.28 (1 H, m, H-16); δ_C (75 MHz; CDCl$_3$) −5.2 (–SiCH$_3$), −4.9 (–SiCH$_3$), −4.8 (–SiCH$_3$), 11.9 (C-18), 16.7 (C-11), 18.1 (–Si–*C*(CH$_3$)$_3$), 18.4 (–Si–*C*(CH$_3$)$_3$), 24.2 (C-12), 25.9 (–Si–C(*C*H$_3$)$_3$), 26.0 (–Si–C(*C*H$_3$)$_3$), 27.4 and 33.9 (C-1 and C-2), 38.0 (C-4), 39.0 (C-14), 39.3 (C-13), 44.0 (C-15), 49.3 (C-9), 51.3 and 51.5 (C-5 and C-6), 51.7 (–CO$_2$*C*H$_3$), 51.8 (C-8), 62.8 (C-3), 72.2 (C-16), 96.4 (C-10), 174.8 (C-19), 179.4 (C-7); *m*/*z* (EI) 565.3381 (M$^+$−15 $C_{30}H_{53}O_6Si_2$ requires 565.3381), 549 (4%), 533 (5), 523 (100), 491 (96) 463 (24), 435 (11), 401 (10), 359 (12), 345 (16), 303 (12), 183 (16), 157 (11), 73 (42).

ent-4α-Bromo-3,16α-bis-*tert*-butyldimethylsilyloxy-10β-hydroxy-3,4-seco-17,20-dinor-4β-gibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (27)

LDA (0.5 M) in THF (2.60 mL, 1.30 mmol) was added dropwise to a stirred solution of **16** (500 mg, 0.86 mmol) in THF (5.0 mL) at −78 °C, then after 25 min tetrabromomethane (713 mg, 2.15 mmol) in THF (2.0 mL) was added dropwise over 5 min. After a further 16 min the reaction was quenched with saturated aq. NH$_4$Cl (2.5 mL) at −78 °C and allowed to warm to rt, then diluted with EtOAc (25 mL) and washed with water (3 × 20 mL). The combined aqueous layers were extracted with EtOAc (2 × 15 mL), the combined organic extracts washed with brine (40 mL) and dried (MgSO$_4$). Concentration *in vacuo* and column chromatography on silica (7% EtOAc and 93% hexane increasing to 10% EtOAc) afforded the title compound (532 mg, 94%) as a pale brown oil. ν_{max} (thin film)/cm^{-1} 3531, 2953, 2930, 2894, 2857, 1774, 1735, 1471, 1462, 1379, 1359, 1249, 1170, 1097, 1067, 891, 836, 776; δ_H (300 MHz; CDCl$_3$) 0.01 (6 H, s, –SiCH$_3$), 0.05 (6 H, s, –SiCH$_3$), 0.87 (9 H, s, –Si*t*-Bu), 0.89 (9 H, s, –Si*t*-Bu), 1.07–1.78 (9 H, m), 1.92 (3 H, s, H-18), 1.96–2.24 (5 H, m), 2.69 (1 H, d, *J* 2.2, H-6), 3.56 (1 H, d, *J* 2.2, H-5), 3.65 (2 H, t, *J* 6.0, H-3), 3.70 (3 H, s, –CO$_2$CH$_3$), 4.28 (1 H, m, H-16); δ_C (75 MHz; CDCl$_3$) −5.2 (–SiCH$_3$), −4.9 (–SiCH$_3$), −4.8 (–SiCH$_3$), 16.4 (C-11), 18.1 (–Si–*C*(CH$_3$)$_3$), 18.4 (–Si–*C*(CH$_3$)$_3$), 24.6 (C-12), 25.9 (–Si–C(*C*H$_3$)$_3$), 26.0 (–Si–C(*C*H$_3$)$_3$), 27.6 (C-18), 28.0 and 33.3 (C-1 and C-2), 39.2 (C-13), 39.4 (C-14), 43.6 (C-15), 48.9 (C-9), 51.6 (C-8), 52.0 (–CO$_2$*C*H$_3$), 53.6 (C-6), 55.8 (C-4), 59.1 (C-5), 62.9 (C-3), 71.9 (C-16), 97.3 (C-10), 173.6 (C-19), 174.8 (C-7); *m*/*z* (EI) 603.1999 (M$^+$−57 $C_{27}H_{46}O_6{}^{81}BrSi_2$ requires 603.1996), 601.2016 (M$^+$−57 $C_{27}H_{46}O_6{}^{79}BrSi_2$ requires 601.2016), 585/583 (14%), 571/569 (50), 543/541 (13), 523/521 (46), 489 (86), 461 (39), 437 (22), 389 (34), 357 (20), 315 (38), 273 (32), 257 (24), 243 (30), 227 (33), 211 (29), 183 (44), 155 (38), 143 (24), 129 (38), 89 (27), 73 (79), 59 (25).

ent-3,16*α*-Bis-*tert*-butyldimethylsilyloxy-10β-hydroxy-3,4-seco-17,20-dinor-4β-gibberellane-4(18)-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (17)

To a stirred solution of the bromide **27** prepared above (370 mg, 0.56 mmol) in toluene (7.5 mL) was added freshly distilled DBU (0.42 mL, 2.81 mmol), then the mixture heated to 70 °C for 18 h, after which a further addition of DBU (0.21 mL, 1.40 mmol) was made. After a total reaction time of 24.5 h the reaction mixture was cooled to rt, diluted with EtOAc (30 mL) and washed with 1.0 M HCl (3 × 25 mL). The combined aqueous layers were extracted with EtOAc (2 × 25 mL), then the combined organic extracts washed with saturated NaHCO$_3$ (3 × 25 mL). The combined aqueous layers were extracted with EtOAc (2 × 25 mL), then the combined organic layers washed with brine (50 mL) and dried (MgSO$_4$). Concentration *in vacuo* and column chromatography on silica (5% EtOAc and 95% hexane) afforded **17** (532 mg, 94%) as a yellow oil. ν_{max} (thin film)/cm^{-1} 3509, 2952, 2929, 2895, 2857, 1763, 1733, 1659, 1472, 1463, 1359, 1273, 1255, 1192, 1168, 1097, 1065, 1006, 968, 920, 892, 835, 775, 734, 665, 615; δ_H (300 MHz; CDCl$_3$) 0.01 (6 H, s, –SiCH$_3$), 0.04 (6 H, s, –SiCH$_3$), 0.88 (9 H, s, –Si*t*-Bu), 0.89 (9 H, s, –Si*t*-Bu), 1.06–2.22 (14 H, m), 2.48 (1 H, d, *J* 0.9, H-6), 3.45 (1 H, d, *J* 1.2, H-5), 3.60 (2 H, m, H-3), 3.70 (3 H, s, –CO$_2$CH$_3$), 4.29 (1 H, m, H-16), 5.67 (1 H, d, *J* 2.2, H-18), 6.27 (1 H, d, *J* 2.6, H′-18); δ_C (75 MHz; CDCl$_3$) −5.2 (–SiCH$_3$), −4.9 (–SiCH$_3$), −4.8 (–SiCH$_3$), 16.6 (C-11), 18.1 (–Si–*C*(CH$_3$)$_3$), 18.4 (–Si–*C*(CH$_3$)$_3$), 24.9 (C-12), 25.9 (–Si–C(*C*H$_3$)$_3$), 26.0 (–Si–C(*C*H$_3$)$_3$), 27.1, 27.6 and 35.0 (C-1, C-2 and C-14), 39.5 (C-13), 43.4 (C-15), 50.2 (C-9), 50.6 (C-6), 51.8 (–CO$_2$*C*H$_3$), 52.6 (C-8), 60.9 (C-5), 62.8 (C-3), 72.0 (C-16), 95.4 (C-10), 123.3 (C-18), 141.1 (C-4), 170.4 (C-19), 174.1 (C-7); *m*/*z* (EI) 521.2760 (M$^+$−57 $C_{27}H_{45}O_6Si_2$ requires 521.2755), (LRMS ESI+) 695 (22%), 694 (28), 693 (53), 581 (24), 580 (47), 579 (100), 551 (4).

ent-18-Allyloxy-3,16α-bis-*tert*-butyldimethylsilyloxy-10β-hydroxy-3,4-seco-17,20-dinor-4β-gibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (18)

To a stirred solution of **17** (200 mg, 0.35 mmol) in allyl alcohol (3.0 mL) was added DBU (0.52 mL, 3.5 mmol). After 1 h, 1.0 M HCl (8 mL) was added, and the reaction mixture then poured into a bilayer of EtOAc (20 mL) and water (20 mL), the organic layer separated and washed with water (3 × 7 mL). The combined aqueous layers were extracted with EtOAc (3 × 15 mL), then the combined organic extracts washed with brine (40 mL) and dried (MgSO$_4$). Concentration *in vacuo* and column chromatography on silica (5% EtOAc and 95% hexane) afforded **9** (78 mg, 58% based on 63% conversion) as an oil. ν_{max} (thin film)/cm^{-1} 2952, 2929, 2895, 2857, 1767, 1733, 1471, 1463, 1445, 1360, 1332, 1251, 1195, 1172, 1098, 1006, 977, 920, 892, 836, 775, 666; δ_H (300 MHz; CDCl$_3$) 0.01 (6 H, s, –SiCH$_3$), 0.04 (6 H, s, –SiCH$_3$), 0.88 (9 H, s, –Si*t*-Bu), 0.89 (9 H, s, –Si*t*-Bu), 1.07–2.24 (14 H, m), 2.43 (1 H, s, H-6), 2.66 (1 H, dd, *J* 4.7 and 9.7, H-4), 2.91 (1 H, d, *J* 3.8, H-5), 3.59 (2 H, t, *J* 6.5, H-3), 3.68 (5 H, m, –CO$_2$CH$_3$ and H-18), 3.98 (2 H, dd, *J* 1.3, 5.5, H-1′), 4.29 (1 H, m, H-16), 5.16 (1 H, tdd, *J* 1.3, 1.4, 10.3, H-3′), 5.23 (1 H, tdd, *J* 1.6, 1.6, 17.2, H′-3′), 5.85 (1 H, m, H-2′); δ_C (75 MHz; CDCl$_3$) −5.2 (–SiCH$_3$), −4.9 (–SiCH$_3$), −4.8 (–SiCH$_3$), 16.9 (C-11), 18.1 (–Si–*C*(CH$_3$)$_3$), 18.4 (–Si–*C*(CH$_3$)$_3$), 25.0 (C-12), 25.9 (–Si–C(*C*H$_3$)$_3$), 26.0 (–Si–C(*C*H$_3$)$_3$), 27.6 and 35.7 (C-1 and C-2), 39.3 (C-14), 39.5 (C-13), 43.6 (C-15), 49.4 (C-9), 50.0 (C-6), 51.7 (C-5), 51.9 (–CO$_2$*C*H$_3$), 52.6 (C-8), 59.8 (C-4), 63.2 (C-3), 69.3 (C-18 or C-1′), 71.8 (C-16), 72.2 (C-18 or C-1′), 97.6 (C-10), 117.2 (C-3′), 134.0 (C-2′), 174.4 (C-19), 177.1 (C-7); *m*/*z* (EI) 579.3174 (M$^+$−57 $C_{30}H_{51}O_7Si_2$ requires 579.3173), (LRMS

ESI+) 753 (9%), 752 (18), 751 (22), 659 (3), 654 (13), 639 (17), 638 (44), 637 (100), 242 (19).

ent-16α-*tert*-Butyldimethylsilyloxy-3,10β-Dihydroxy-3,4-seco-17,20-dinorgibberell-4(18)-ene-7,19-dioic acid 7-methyl ester 19,10-lactone

To a stirred solution of **17** (525 mg, 0.797 mmol) in THF (10.0 mL) at 0 °C was added dropwise 1.0 M TBAF in THF (2.39 mL, 2.39 mmol). After 1.3 h, this was poured into a bilayer of EtOAc (25 mL) and water (25 mL), the organic layer separated and washed with water (3 × 10 mL). The combined aqueous layers were extracted with EtOAc (2 × 15 mL), and the combined organic extracts washed with brine (40 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (25% EtOAc and 75% hexane, increasing to 100% EtOAc) gave the title compound as a white foam (264 mg, 71%) ν_{max} (thin film)/cm^{-1} 3456, 2941, 2930, 2857, 1758, 1734, 1659, 1471, 1444, 1404, 1358, 1275, 1256, 1194, 1169, 1097, 1064, 970, 920, 892, 835, 816, 776, 733, 667, 617; δ_H (300 MHz; $CDCl_3$) 0.00 (3 H, s, –$SiCH_3$), 0.01 (3 H, s, –$SiCH_3$), 0.87 (9 H, s, –Si*t*-Bu), 1.04–1.80 (11 H, m), 2.03–2.23 (3 H, m), 2.49 (1 H, d, *J* 1.0, H-6), 3.46 (1 H, d, *J* 1.0, H-5), 3.67 (2 H, td, *J* 2.3, 6.3, H-3), 3.70 (3 H, s, –CO_2CH_3), 4.28 (1 H, m, H-16), 5.68 (1 H, d, *J* 2.3, H-18), 6.26 (1 H, d, *J* 2.6, H′-18); δ_C (75 MHz; $CDCl_3$) −4.9 (–$SiCH_3$), −4.8 (–$SiCH_3$), 16.7 (C-11), 18.1 (–Si–$C(CH_3)_3$), 24.9 (C-12), 25.9 (–Si–$C(CH_3)_3$), 27.1 and 35.0 (C-1 and C-2), 39.5 and 41.0 (C-13, C-14 and C-15), 50.2 (C-9), 50.6 (C-6), 51.9 (–CO_2CH_3), 52.7 (C-8), 60.8 (C-5), 62.7 (C-3), 71.9 (C-16), 95.2 (C-10), 123.4 (C-18), 140.9 (C-4), 170.3 (C-19), 174.3 (C-7); *m/z* (EI) 407.1890 ($M^+ - 57$ $C_{21}H_{31}O_6Si$ requires 407.1890), 389 (6%), 375 (11), 365 (6), 357 (14), 347 (20), 329 (9), 315 (12), 283 (26), 255 (38), 245 (16), 227 (26), 213 (48), 199 (10), 185 (24), 167 (11), 157 (20), 141 (17), 129 (22), 115 (18), 105 (21), 91 (64), 73 (89), 59 (34).

ent-16α-*tert*-Butyldimethylsilyloxy-10β-hydroxy-3-oxo-3,4-seco-17,20-dinorgibberell-4(18)-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (19)

To a stirred solution of the 3-ol prepared above (99 mg, 0.21 mmol) in CH_2Cl_2 (2.5 mL) was added Dess–Martin periodinane (187 mg, 0.42 mmol). After 2.5 h, saturated $NaHCO_3$ (1.25 mL) and 1.0 M $Na_2S_2O_3$ (1.25 mL) were added, and once both layers had turned clear the reaction was poured into a bilayer of EtOAc (7.5 mL) and water (7.5 mL), the organic layer separated and washed with water (2 × 3 mL). The combined aqueous extracts were back-extracted with EtOAc (2 × 5 mL), then the combined organic layers washed with brine (10 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (25% EtOAc and 75% hexane, increasing to 33% EtOAc) afforded **19** (98 mg, *ca.* 100%) as an oil. ν_{max} (thin film)/cm^{-1} 2951, 2930, 2896, 2857, 1761, 1727, 1658, 1442, 1357, 1273, 1251, 1193, 1169, 1096, 1067, 968, 921, 892, 835, 815, 775; δ_H (300 MHz; $CDCl_3$) 0.01 (6 H, s, –$SiCH_3$), 0.88 (9 H, s, –Si*t*-Bu), 1.04–2.62 (15 H, m), 3.41 (1 H, m, H-5), 3.71 (3 H, s, –CO_2CH_3), 4.29 (1 H, m, H-16), 5.71 (1 H, d, *J* 2.3, H-18), 6.30 (1 H, d, *J* 2.6, H′-18) 9.76 (1 H, s, H-3); δ_C (75 MHz; $CDCl_3$) −4.9 (–$SiCH_3$), −4.8 (–$SiCH_3$), 16.7 (C-11), 18.1 (–Si–$C(CH_3)_3$), 24.9 (C-12), 25.9 (–Si–$C(CH_3)_3$), 27.6 and 30.1 (C-1 and C-2), 38.6 (C-15), 39.4 (C-13), 43.4 (C-14), 50.2 (C-9), 50.3 (C-6), 52.0 (–CO_2CH_3), 52.7 (C-8), 60.7 (C-5), 71.8 (C-16), 94.2 (C-10), 124.1 (C-18), 140.3 (C-4), 169.9 (C-19), 174.1 (C-7), 200.4 (C-3); *m/z* (EI) 405 (37%), 387 (8), 373 (52), 355 (59), 327 (12), 313 (26), 299 (8), 281 (20), 255 (42), 239 (13), 225 (31), 207 (14), 179 (13), 155 (11), 131 (42), 105 (12), 91 (21), 75 (100).

ent-16α-*tert*-Butyldimethylsilyloxy-18-allyloxy-3α,10β-dihydroxy-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (20)

To a stirred solution of **19** (107 mg, 0.23 mmol) in allyl alcohol (2.5 mL) was added DBU (346 μL, 2.3 mmol). After 1 h the reaction was neutralised with 1.0 M HCl, then concentrated *in vacuo.* The residue was taken up in a bilayer of EtOAc (10 mL) and water (10 mL), the organic layer separated and washed with water (3 × 4 mL). The combined aqueous extracts were back-extracted with EtOAc (2 × 6 mL), then the combined organic layers washed with brine (10 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (15% EtOAc and 85% hexane, increasing to 33% EtOAc) afforded **20** (30 mg, 27%) then *epi*-**20** (25 mg, 23%).

20: ν_{max} (thin film)/cm^{-1} 3504, 2951, 2932, 2881, 2857, 1773, 1737, 1462, 1471, 1436, 1375, 1250, 1192, 1164, 1095, 1022, 977, 935, 881, 835, 776, 666; δ_H (300 MHz; $CDCl_3$) 0.01 (6 H, s, –$SiCH_3$), 0.87 (9 H, s, –Si*t*-Bu), 1.21–2.03 (13 H, m), 2.19 (1 H, m, H-13), 2.62 (1 H, d, *J* 10.3, H-6), 3.41 (1 H, d, *J* 10.2, H-5), 3.50 (1 H, d, *J* 9.8, H-18), 3.67 (3 H, s, –CO_2CH_3), 3.86 (1 H, d, *J* 9.8, H′-18), 3.91 (2 H, m, H-1′), 4.14 (1 H, m, H-3), 4.19 (1 H, m, H-16), 5.19 (1 H, dd, *J* 1.4, 5.1, H-3′), 5.23 (1 H, tdd, *J* 1.4, 1.6, 11.4, H′-3′), 5.80 (1 H, m, H-2′); δ_C (75 MHz; $CDCl_3$) −4.8 (–$SiCH_3$), 15.6 (C-11), 18.2 (–Si–$C(CH_3)_3$), 18.4 (C-12), 25.9 (–Si–$C(CH_3)_3$), 27.1 and 27.2 (C-1 and C-2), 36.6 (C-14), 37.9 (C-13), 47.0 (C-15), 49.9 (C-9), 51.3 (C-8), 51.7 (–CO_2CH_3), 52.8 (C-6), 55.5 (C-5), 57.7 (C-4), 70.6 (C-3), 71.5 (C-18), 72.6 (C-16), 72.7 (C-1′), 96.1 (C-10), 118.0 (C-3′), 133.1 (C-2′), 172.9 (C-19), 174.9 (C-7); *m/z* (EI) 519.2781 (M^+ $C_{28}H_{43}O_7$ Si requires 519.2778), 505 (4%), 489 (5), 463 (100), 445 (7), 431 (21), 403 (4), 385 (4), 373 (7), 357 (4), 345 (6), 315 (6), 269 (10), 241 (9), 225 (9), 209 (7), 183 (10), 167 (9), 141 (9), 129 (12), 115 (7), 91 (11), 75 (42), 59 (12).

epi-**20**: ν_{max} (thin film)/cm^{-1} 3470, 2951, 2931, 2881, 2857, 1774, 1736, 1471, 1462, 1436, 1352, 1255, 1191, 1164, 1100, 986, 930, 883, 834, 775; δ_H (300 MHz; $CDCl_3$) 0.00 (6 H, s, –$SiCH_3$), 0.86 (9 H, s, –Si*t*-Bu), 1.14–2.24 (14 H, m), 2.60 (1 H, d, *J* 10.0, H-6), 2.79 (1 H, d, *J* 9.8, H-5), 3.55 (1 H, d, *J* 10.1, H-18), 3.66 (3 H, s, –CO_2CH_3), 3.85 (1 H, d, *J* 10.1, H′-18), 3.89 (2 H, m, H-1′), 3.95 (1 H, m, H-3), 4.18 (1 H, m, H-16), 5.14 (1 H, dd, *J* 1.5,8.9, H-3′), 5.21 (1 H, tdd, *J* 1.6, 1.6, 17.3, H′-3′), 5.80 (1 H, m, H-2′); δ_C (75 MHz; $CDCl_3$) −4.8 (–$SiCH_3$), 15.6 (C-11), 18.2 (–Si–$C(CH_3)_3$), 18.6 (C-12), 25.9 (–Si–$C(CH_3)_3$), 29.1 and 29.9 (C-1 and C-2), 36.6 (C-14), 37.7 (C-13), 46.9 (C-15), 51.7 (–CO_2CH_3), 52.1 (C-8), 52.8 (C-9), 55.0 (C-6), 55.1 (C-5), 58.4 (C-4), 66.4 (C-18), 69.9 (C-3), 72.4 (C-1′), 72.7 (C-16), 94.2 (C-10), 117.1 (C-3′), 134.0 (C-2′), 173.1 (C-19), 175.0 (C-7); *m/z* (EI) 543.2755 ($M + Na^+$ $C_{28}H_{44}O_7SiNa$ requires 543.2754), 505 (5%), 489 (4), 463 (100), 445 (5), 431 (14), 413 (13), 373 (5), 345 (5), 329 (4), 269 (6), 253 (8), 225 (7), 197 (6), 181 (10), 155 (12), 142 (6), 129 (9), 91 (10), 75 (35), 59 (11).

ent-18-Benzyloxy-16α-*tert*-butyldimethylsilyloxy-3α,10β-dihydroxy-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (21)

To a stirred solution of **19** (1.00 g, 2.16 mmol) in benzyl alcohol (7.5 mL) was added DBU (3.24 mL, 21.65 mmol). After 2.5 h this was poured into a bilayer of 1.0 M HCl (40 mL) and EtOAc (75 mL), the organic layer separated and washed with water (3 × 20 mL). The combined aqueous extracts were back-extracted with EtOAc (2 × 40 mL), then the combined organic layers washed with brine (90 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (15% EtOAc and 85% hexane, increasing to 33% EtOAc) afforded **21** (376 mg, 31%) then *epi*-**21** (509 mg, 41%).

21: ν_{max} (thin film)/cm^{-1} 3508, 2951, 2930, 2857, 1772, 1736, 1471, 1453, 1435, 1361, 1249, 1193, 1164, 1095, 1021, 978, 936, 882, 834, 775, 737, 697, 667; δ_H (300 MHz; $CDCl_3$) 0.02 (6 H, s, –$SiCH_3$), 0.88 (9 H, s, –Si*t*-Bu), 1.23–2.22 (14 H, m), 2.65 (1 H, d, *J* 10.3, H-6), 3.47 (1 H, d, *J* 10.3, H-5), 3.55 (1 H, d, *J* 9.8, H-18), 3.62 (3 H, s, –CO_2CH_3), 3.95 (1 H, d, *J* 9.8, H′-18), 4.14 (1 H, d, *J* 3.4, H-3), 4.20 (1 H, m, H-16), 4.42 (1 H, d, *J* 11.6, benzyl-H), 4.47 (1 H, d, *J* 11.4, benzyl-H′) 7.27–7.38 (5 H, m, aromatic-H); δ_C (75 MHz; $CDCl_3$) −4.7 (–$SiCH_3$), 15.6 (C-11), 18.2 (–Si–$C(CH_3)_3$), 18.4 (C-12), 25.9 (–Si–$C(CH_3)_3$), 27.1 and 27.2 (C-1 and C-2), 36.5 (C-14), 37.9 (C-13), 47.0 (C-15), 49.9 (C-9), 51.3 (C-8), 51.7 (–CO_2CH_3), 52.8 (C-6), 55.5 (C-5), 57.7 (C-4), 70.5 (C-3), 71.8 (C-18), 72.6 (C-16), 74.1 (benzyl-C), 96.1 (C-10), 127.5, 128.0, 128.5 and 136.6 (aromatic-C), 173.0 (C-19), 174.9 (C-7); *m*/*z* (EI) 539.2826 (M^+−57 $C_{31}H_{43}O_6Si$ requires 539.2829), 513 (85%), 495 (4), 481 (24), 453 (5), 444 (16), 431 (4), 405 (7), 373 (9), 345 (5), 315 (5), 297 (6), 271 (6), 253 (7), 225 (6), 181 (7), 155 (8), 145 (5), 129 (9), 107 (12), 91 (100), 75 (29), 59 (9).

epi-**21**: ν_{max} (thin film)/cm^{-1} 3369, 2951, 2931, 2880, 2858, 1773, 1735, 1471, 1455, 1437, 1369, 1249, 1165, 1104, 1028, 984, 911, 883, 834, 774, 734, 696; δ_H (300 MHz; $CDCl_3$) 0.01 (6 H, s, –$SiCH_3$), 0.87 (9 H, s, –Si*t*-Bu), 1.18–2.22 (14 H, m), 2.67 (1 H, d, *J* 9.8, H-6), 2.80 (1 H, d, *J* 9.8, H-5), 3.55 (3 H, s, –CO_2CH_3), 3.58 (1 H, d, *J* 10.3, H-18), 3.94 (1 H, d, *J* 10.1, H′-18), 4.01 (1 H, m, H-3), 4.19 (1 H, m, H-16), 4.41 (1 H, d, *J* 12.0, benzyl-H), 4.48 (1 H, d, *J* 12.0, benzyl-H′) 7.25–7.36 (5 H, m, aromatic-H); δ_C (75 MHz; $CDCl_3$) −4.7 (–$SiCH_3$), 15.7 (C-11), 18.2 (–Si–$C(CH_3)_3$), 18.7 (C-12), 25.9 (–Si–$C(CH_3)_3$), 29.0 and 29.9 (C-1 and C-2), 36.7 (C-14), 37.8 (C-13), 46.9 (C-15), 51.7 (–CO_2CH_3), 52.2 (C-8), 52.8 (C-9), 55.0 (C-6), 55.1 (C-5), 58.5 (C-4), 66.5 (C-18), 69.8 (C-3), 72.7 (C-16), 73.5 (benzyl-C), 94.3 (C-10), 127.4, 127.6, 128.3 and 137.6 (aromatic-C), 173.1 (C-19), 174.9 (C-7); *m*/*z* (EI) 571.3090 (MH^+ $C_{32}H_{47}O_7Si$ requires 571.3091), 555 (21%), 539 (12), 513 (78), 481 (14), 463 (2), 444 (12), 405 (7), 373 (14), 355 (6), 312 (5), 281 (3), 269 (8), 209 (7), 181 (9), 155 (9), 145 (4), 129 (9), 107 (13), 91 (100), 75 (32), 59 (8).

ent-16α-*tert*-Butyldimethylsilyloxy-3α,10β,18-trihydroxy-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (23) 3,18-acetonide

To a stirred solution of **20** (25 mg, 48 μmol) in aqueous EtOH (4 mL) was added $RhCl_3$ (3 mg, 14 μmol) and DABCO (16 mg, 144 μmol), and this mixture then heated to reflux for 17 h. The reaction mixture was then allowed to cool to rt, and 1.0 M HCl (4 mL) added. After 50 min the solvent was removed *in vacuo*, the resulting residue then taken up in a bilayer of 20% 2-butanol in EtOAc (10 mL) and water (10 mL). The aqueous layer was extracted with 20% 2-butanol in EtOAc (2 × 10 mL), then the combined organic layers washed with brine (10 mL), dried ($MgSO_4$) then concentrated *in vacuo* and purified further through a short column of silica (100% EtOAc). The resulting residue was taken up in CH_2Cl_2 (400 μL), and PPTS (4 mg, 15 μmol) then 2,2-dimethoxypropane (30 μL, 246 μmol) were added. After 5.5 h, a second addition of PPTS (4 mg, 15 μmol) and 2,2-dimethoxypropane (15 μL, 123 μmol) was made. After a further 18.5 h, this was diluted with 5% 2-butanol in EtOAc (10 mL), and washed with saturated $NaHCO_3$ (5 mL) then brine (5 mL). Concentration *in vacuo* and column chromatography on silica (33% EtOAc and 67% hexane, increasing to 100% EtOAc) afforded **23** 3,18-acetonide (10.4 mg, 52%) as an oil. ν_{max} (thin film)/cm^{-1} 3468, 2943, 2875, 1769, 1735, 1455, 1436, 1383, 1278, 1257, 1191, 1170, 1091, 1071, 1055, 1030, 997, 963, 944, 915, 866, 851, 732; δ_H (300 MHz; $CDCl_3$) 1.26–1.39 (4 H, m), 1.42 (3 H, s, acetonide-Me), 1.46 (3 H, s, acetonide-Me′), 1.57–2.19 (9 H, m), 2.31 (1 H, m, H-13), 2.59 (1 H, d, *J* 9.8, H-6), 3.37 (1 H, d, *J* 9.8, H-5), 3.61 (1 H, d, *J* 12.2, H-18), 3.72 (3 H, s, –CO_2CH_3), 4.10–4.14 (2 H, m, H′-18 and H-3), 4.32 (1 H, m, H-16); δ_C (75 MHz; $CDCl_3$) 15.5 (C-11), 18.2, 19.1 and 29.9 (C-1, C-2 and C-12), 27.8 (acetonide-Me), 29.5 (acetonide-Me′), 37.0 (C-14), 37.5 (C-13), 46.3 (C-15), 50.2 (C-9), 51.8 (C-8), 51.9 (–CO_2CH_3), 53.4 (C-6), 53.5 (C-4), 56.3 (C-5), 61.5 (C-18), 68.1 (C-3), 72.4 (C-16), 96.0 (C-10), 99.9 (acetonide-CMe_2), 172.8 (C-19), 174.6 (C-7); *m*/*z* (EI) 406.1998 (M^+ $C_{22}H_{30}O_7$ requires 406.1992), (LRMS ESI+) 429 (32%), 407 (100), 389 (7), 367 (12), 349 (13), 331 (18), 102 (30).

ent-16α-18-Benzyloxy-*tert*-butyldimethylsilyloxy-10β-hydroxy-3β-methanesulfonyloxy-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone

To a stirred solution of 3-*epi*-**21** (100 mg, 0.18 mmol) in pyridine (2 mL) was added methanesulfonyl chloride (27 μL, 0.35 mmol). After 40 min, a second addition of methanesulfonyl chloride (27 μL, 0.35 mmol) was made, and after a further 50 min the reaction mixture was poured into 2.0 M HCl (4 mL) and EtOAc (10 mL). The organic layer was washed with water (4 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 5, increasing to EtOAc–hexane 1 : 3) afforded the title compound (101 mg, 87%) as an oil. ν_{max} (cm^{-1}) 2951, 2931, 2882, 2857, 1777, 1734, 1471, 1462, 1437, 1361, 1250, 1175, 1105, 1087, 959, 944, 836, 776, 750, 698. δ_H (300 MHz; $CDCl_3$) −0.02 (6 H, s, –$SiCH_3$), 0.84 (9 H, s, –Si*t*-Bu), 1.15–2.22 (13 H, m), 2.46 (1 H, m, H-13), 2.75 (2 H, s, H-5 and H-6), 2.85 (3 H, s, –OSO_2CH_3), 3.46–3.50 (4 H, m, –CO_2CH_3 and H-18), 3.88 (1 H, d, *J* 10.1, H′-18), 4.16 (1 H, m, H-16), 4.37 (1 H, d, *J* 11.6, H-1′), 4.42 (1 H, d, *J* 11.7, H′-1′), 4.92 (1 H, dd, *J* 10.7, *J* 6.3, H-3), 7.22–7.33 (5 H, m, H-2″–H-6″). δ_C (75 MHz; $CDCl_3$) δ −4.8 (–$SiCH_3$), 15.7 (C-11), 18.2 (–Si$C(CH_3)_3$), 18.7 (C-12), 25.9 (–Si$C(CH_3)_3$), 27.4 and 29.4 (C-1 and C-2), 37.0 (C-14), 37.8 (C-13), 38.6 (–OSO_2CH_3), 46.8 (C-15), 51.8 (–CO_2CH_3), 52.2 (C-8), 52.7 (C-9), 54.8 and 55.3 (C-5 and C-6), 56.8 (C-4), 65.7 (C-18), 72.5 (C-16), 73.7 (C-1′), 77.2 (C-3), 94.2 (C-10), 127.7 (C-2″, C-4″ and C-6″), 128.2 (C-3″ and C-5″), 137.1 (C-1″), 172.6 (C-19), 173.0 (C-7). *m*/*z* (ESI) 750 (8%), 738 (6), 672 (10), 671 (29), 650 (41), 649

(100), 637 (62), 617 (5), 523 (7), 391 (18), 327 (6), 305 (10), 279 (11), 273 (19), 243 (13), 242 (68), 214 (47), 191 (7), 174 (11), 173 (20), 158 (13), 142 (22), 116 (33). HRMS (EI) *m*/*z* calcd for $M^+ - C_4H_9$, $C_{29}H_{39}O_9SiS$: 591.2084; found: 591.2086.

ent-18-Benzyloxy-3α-acetoxy-16α-*tert*-butyldimethylsilyloxy-10β-hydroxy-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone and *ent*-18-Benzyloxy-16α-*tert*-butyldimethylsilyloxy-10β-hydroxy-17,20-dinorgibberell-2-ene-7,19-dioic acid 7-methyl ester 19,10-lactone

To a stirred solution of 18-crown-6 ether (135 mg, 0.51 mmol) and cesium acetate (89 mg, 0.47 mmol) in DMF (0.5 mL) was added activated 3 Å molecular sieves, and the resulting mixture was heated to 100 °C. After 45 min, the mixture was allowed to cool to 25 °C, and the mesylate prepared above (101 mg, 0.155 mmol) was added in DMF (2 mL). The reaction mixture was heated to 125 °C for 6 h, 110 °C for 18 h, and then to 125 °C for a further 3 h. After a total reaction time of 27 h, the reaction mixture was allowed to cool then diluted with EtOAc (10 mL) and washed with brine (5 mL), and then with water (5 mL). The aqueous layer was back-extracted with EtOAc (5 mL), and the combined organic layers were then washed with brine (10 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 15, increasing to 1 : 1) afforded the 3β-acetate (3 mg, 3%) as an oil, followed by the Δ^2 alkene (15 mg, 18%) as an oil, and then starting material (12 mg, 12%).

3β-Acetate. δ_H (300 MHz; $CDCl_3$) 0.02 (6 H, s, $-SiCH_3$), 0.88 (9 H, s, –Si*t*-Bu), 1.16–2.18 (13 H, m), 2.03 (3 H, s, $-OCOCH_3$), 2.20 (1 H, m, H-13), 2.99 (1 H, d, *J* 10.8, H-6), 3.27 (1 H, d, *J* 10.7, H-5), 3.45 (3 H, s, $-CO_2CH_3$), 3.52 (1 H, d, *J* 9.8, H-18), 3.70 (1 H, d, *J* 9.7, H′-18), 4.21 (1 H, m, H-16), 4.37 (1 H, d, *J* 12.0, H-1′), 4.38 (1 H, d, *J* 12.2, H′-1′), 5.05 (1 H, m, H-3), 7.22–7.34 (5 H, m, H-2″–H-6″).

Δ^2 Alkene. δ_H (300 MHz; $CDCl_3$) 0.01 (3 H, s, $-SiCH_3$), 0.01 (3 H, s, $-SiCH_3$), 0.87 (9 H, s, –Si*t*-Bu), 1.15–1.97 (13 H, m), 2.20 (1 H, m, H-13), 2.38 (1H, dt, *J* 18.6, *J* 2.72, H-1β), 2.63 (1H, ddd, *J* 18.7, *J* 3.3, *J* 1.7, H-1α), 2.85 (1 H, d, *J* 10.1, H-6), 2.90 (1 H, d, *J* 10.1, H-5), 3.50 (3 H, m, $-CO_2CH_3$), 3.67 (1 H, d, *J* 10.0, H-18), 3.73 (1 H, d, *J* 9.8, H′-18), 4.20 (1 H, m, H-16), 4.45 (1 H, d, *J* 12.2, H-1′), 4.49 (1 H, d, *J* 12.2, H′-1′), 5.63 (1 H, dt, *J* 9.4, *J* 1.8, H-3), 5.86 (1 H, dt, *J* 9.2, *J* 3.2, H-2), 7.24–7.35 (5 H, m, H-2″–H-6″).

ent-18-Benzyloxy-16α-*tert*-butyldimethylsilyloxy-10β-hydroxy-3-oxo-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (24)

To a stirred solution of 3-*epi*-**21** (51 mg, 0.09 mmol) in CH_2Cl_2 (3 mL) was added Dess–Martin periodinane (99 mg, 0.23 mmol). After 30 min, saturated aqueous $NaHCO_3$ (1.5 mL) and 1.0 M $Na_2S_2O_3$ (1.5 mL) were added. Once both layers had turned clear, the reaction was poured into EtOAc (12 mL) and water (12 mL), and the organic layer then separated and washed with water (2 × 5 mL). The combined aqueous extracts were back-extracted with EtOAc (2 × 7.5 mL), and the combined organic layers were then washed with brine (10 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 4) afforded **24** (38 mg, 75%) as an oil. ν_{max} (cm^{-1}) 2927, 2851, 1783, 1733, 1456, 1363, 1323, 1258, 1198, 1162, 1091, 1035, 931, 884, 834, 776, 734, 697. δ_H (300 MHz; $CDCl_3$) 0.01 (3 H, s, $-SiCH_3$), 0.02 (3 H, s, $-SiCH_3$), 0.88 (9 H, s, –Si*t*-Bu), 1.20–2.05 (10 H, m), 2.21 (1 H, m, H-13), 2.50–2.64 (3 H, m), 3.13 (1 H, d, *J* 9.7, H-6), 3.20 (1 H, d, *J* 9.8, H-5), 3.44 (3 H, s, $-CO_2CH_3$), 3.84 (1 H, d, *J* 10.4, H-18), 3.95 (1 H, d, *J* 10.6, H′-18), 4.23 (1 H, m, H-16), 4.43 (1 H, d, *J* 12.0, H-1′), 4.45 (1 H, d, *J* 12.0, H′-1′), 7.25–7.34 (5 H, m, H-2″–H-6″). δ_C (75 MHz; $CDCl_3$) −4.7 ($-SiCH_3$), 15.8 (C-11), 18.2 (–Si*C*(CH_3)$_3$), 18.9 (C-12), 25.9 (–SiC(*C*H_3)$_3$), 29.8 (C-1), 35.0 (C-2), 36.6 (C-14), 37.5 (C-13), 46.7 (C-15), 51.5 ($-CO_2$*C*H_3), 52.5 (C-8), 52.9 (C-6), 54.7 (C-9), 55.2 (C-5), 65.3 (C-4), 66.8 (C-18), 72.7 (C-16), 73.6 (C-1′), 93.7 (C-10), 127.2 (C-4″), 127.4 (C-2″ and C-6″), 128.1 (C-3″ and C-5″), 137.2 (C-1″), 172.6 (C-19), 176.0 (C-7), 199.3 (C-3). *m*/*z* (ESI) 717 (7%), 691 (11), 684 (8), 593 (7), 592 (19), 591 (43), 569 (52), 540 (10), 539 (24), 537 (7), 506 (5), 413 (22), 392 (27), 391 (100), 301 (33), 279 (43), 242 (8), 236 (9), 205 (29), 164 (5), 138 (5), 136 (28), 102 (35). HRMS (EI) calcd for $M^+ - C_4H_9$, $C_{28}H_{35}O_7Si$: 511.2152; found: 511.2156.

ent-16α-*tert*-Butyldimethylsilyloxy-3α,10β-dihydroxy-17,20-dinorgibberell-4(18)-ene-7,19-dioic acid 7-methyl ester 19(4→3β)*abeo*-19,10-lactone (25) and *ent*-18-Benzyloxy-16α-*tert*-butyldimethylsilyloxy-3α,10β-dihydroxy-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19(4→3β)*abeo*-19,10-lactone (26)

To a stirred, dark blue solution of SmI_2 in THF (1.62 mL, 0.05 M, 0.081 mmol) was added a degassed solution of **24** (23 mg, 0.040 mmol) in THF (1.3 mL), followed by degassed H_2O (0.16 mL). Once the reaction mixture had turned yellow, it was poured into 0.1 M HCl (6.5 mL), and then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with water (10 mL), with 1.0 M $Na_2S_2O_3$ (10 mL), with water (10 mL), with brine (10 mL), and then dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 5, increasing to 2 : 7) afforded 3-*epi*-**21** (16 mg, 35%) as an oil, followed by **25** (4 mg, 11%) as an oil, and then **26** (5 mg, 9%) as an oil.

25: ν_{max} (cm^{-1}) 3468, 2951, 2931, 2881, 2856, 1758, 1735, 1656, 1462, 1438, 1373, 1334, 1256, 1169, 1102, 1051, 1002, 935, 902, 873, 835, 776, 751. δ_H (300 MHz; $CDCl_3$) 0.02 (6 H, s, $-SiCH_3$), 0.88 (9 H, s, –Si*t*-Bu), 1.21–2.25 (14 H, m), 2.66 (1 H, d, *J* 11.4, H-6), 3.31 (1 H, s, –OH), 3.35 (1 H, td, *J* 11.4, *J* 2.3, H-5), 3.75 (3 H, s, $-CO_2CH_3$), 4.18 (1 H, m, H-16), 5.01 (1 H, d, *J* 2.1, H-18), 5.45 (1 H, d, *J* 2.6, H′-18). δ_C (75 MHz; $CDCl_3$) −4.7 ($-SiCH_3$), 14.7 (C-11), 18.1 (C-12), 18.2 (–Si*C*(CH_3)$_3$), 25.9 (–SiC(*C*H_3)$_3$), 28.5 (C-1), 30.3 (C-2), 35.8 (C-14), 37.7 (C-13), 46.8 (C-15), 49.3 (C-9), 51.3 (C-8), 51.9 ($-CO_2$*C*H_3), 54.6 (C-6), 56.0 (C-5), 72.8 (C-16), 73.7 (C-3), 91.5 (C-10), 109.9 (C-18), 144.4 (C-4), 173.7 (C-19), 175.2 (C-7). *m*/*z* (EI) 405.1733 ($C_{21}H_{29}O_6Si$, $M^+ - 57$, requires 405.1733), 447 (5%), 405 (100), 359 (4), 317 (6), 286 (17), 227 (8), 129 (5), 75 (32).

26: ν_{max} (cm^{-1}) 3462, 2951, 2931, 2881, 2856, 1756, 1735, 1496, 1471, 1461, 1436, 1368, 1341, 1250, 1169, 1134, 1096, 1027, 1003, 936, 903, 881, 835, 775, 751, 697, 666. δ_H (300 MHz; $CDCl_3$) 0.01 (6 H, s, $-SiCH_3$), 0.87 (9 H, s, –Si*t*-Bu), 1.11–2.21 (14 H, m), 2.46–2.51 (2 H, m, H-4 and H-5), 2.64 (1 H, d, *J* 11.4, H-6), 3.44 (3 H, s, $-CO_2CH_3$), 3.73–3.93 (2 H, m, H-18), 4.19 (1 H, m, H-16), 4.54 (1 H, d, *J* 11.9, H-1′), 4.48 (1 H, d, *J* 11.7, H′-1′), 7.25–7.35 (5 H, m, H-2″–H-6″). δ_C (75 MHz; $CDCl_3$) −4.7 ($-SiCH_3$), 14.9 (C-11), 18.2 (–Si*C*(CH_3)$_3$), 18.7 (C-12), 25.5 (C-1), 25.9 (–SiC(*C*H_3)$_3$), 28.6 (C-2), 36.1 (C-14), 37.8 (C-13), 44.7 (C-4), 46.4 (C-15), 47.2 (C-9), 50.6 (C-8), 51.7 (–CO$_2$*C*H$_3$), 54.5 (C-6), 56.7 (C-5), 68.7 (C-18), 71.8 (C-1′), 72.8 (C-16), 73.7 (C-3), 90.8 (C-10), 127.5 (C-4″), 127.6 and 127.6 (C-2″ and C-6″), 128.3 and 128.5 (C-3″ and C-5″), 137.6 (C-1″), 173.5 (C-19), 177.0 (C-7). *m*/*z* (EI) 539.2819, (C$_{31}$H$_{43}$O$_6$Si, M$^+$–OCH$_3$, requires 539.2829) 570 (M$^+$, 1%), 555 (3), 539 (2), 513 (90), 481 (27), 462 (9), 444 (6), 417 (4), 375 (3), 347 (3), 299 (4), 271 (6), 241 (4), 213 (5), 185 (5), 155 (7), 129 (9), 117 (6), 107 (9), 91 (100), 75 (24).

ent-3,16-Dioxo-10β-hydroxy-3,4-*seco*-17,20-dinorgibberell-4(18)-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (29)

To a stirred solution of **27** (prepared by bromination of **16** (*vide supra*) (50 mg, 76 μmol) in THF (1.0 mL) at 0 °C was added dropwise 1.0 M TBAF in THF (223 mL, 223 μmol). Further additions of TBAF (4 × 76 μL, 76 μmol) were made in batches over 57 h, the reaction mixture having been allowed to warm to rt after 11 h 30 min and then heated to 45 °C after a further 47 h 30 min. The reaction mixture was then diluted with 5% 2-butanol in EtOAc (10 mL) and washed with water (2 × 4 mL), and the combined aqueous layers were extracted with 5% 2-butanol in EtOAc (2 × 3 mL). The combined organic extracts were washed with brine (15 mL), dried (MgSO$_4$) and concentrated *in vacuo* to give the crude diol. To a stirred solution of the resulting crude diol (*ca.* 27 mg, 76 mmol) in CH$_2$Cl$_2$ (2.5 mL) was added Dess–Martin periodinane (100 mg, 228 mmol). After 50 min, saturated aqueous NaHCO$_3$ (1.25 mL) and 1.0 M Na$_2$S$_2$O$_3$ (1.25 mL) were added. Once both layers had turned clear, the reaction was diluted with 5% 2-butanol in EtOAc (10 mL) and washed with water (2 × 5 mL). The combined aqueous extracts were back-extracted with 5% 2-butanol in EtOAc (2 × 3 mL), and the combined organic layers were then washed with brine (10 mL) and dried (MgSO$_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 1) afforded **29** (16 mg, 62%) as an oil. ν_{max} (cm^{-1}) 2950, 2867, 1760, 1728, 1658, 1437, 1405, 1354, 1273, 1198, 1171, 1070, 966, 817, 730. δ_H (300 MHz; CDCl$_3$) 1.75–2.54 (14 H, m), 2.75 (1 H, d, *J* 1.2, H-6), 3.56 (1 H, d, *J* 1.2, H-5), 3.72 (3 H, s, –CO$_2$CH$_3$), 5.81 (1 H, d, *J* 2.3, H-18), 6.38 (1 H, d, *J* 2.6, H′-18), 9.77 (1 H, d, *J* 1.0, H-3). δ_C (75 MHz; CDCl$_3$) 17.1 (C-11), 27.6, 28.8 and 30.5 (C-1, C-2 and C-12), 38.9 (C-14), 46.3 (C-13), 48.2 (C-15), 49.0 (C-9), 49.7 (C-6), 51.5 (C-8), 52.3 (–CO$_2$*C*H$_3$), 60.2 (C-5), 93.8 (C-10), 124.9 (C-18), 139.6 (C-4), 169.4 (C-19), 173.2 (C-7), 200.0 (C-3), 218.1 (C-16). *m*/*z* (EI); 346.1420.0 (M$^+$ C$_{19}$H$_{22}$O$_6$ requires 346.1416), 318 (100), 300 (69), 286 (68), 272 (18), 258 (33), 242 (37), 229 (41), 215 (23), 201 (37), 185 (15), 173 (21), 155 (23), 131 (22), 115 (26), 91 (62).

ent-18-Benzyloxy-3α,10β-Dihydroxy-16-oxo-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (30)

To a stirred solution of **29** (0.92 g, 2.66 mmol) in benzyl alcohol (5 mL) was added DBU (3.98 mL, 26.6 mmol). After 3 h, the reaction mixture was poured into 1.0 M HCl (40 mL) and EtOAc (75 mL), and the organic layer was separated and washed with water (3 × 40 mL). The combined aqueous extracts were back-extracted with EtOAc (2 × 40 mL), and the combined organic layers were then washed with brine (120 mL) and dried (MgSO$_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 9, increasing to 1 : 1) afforded **30** (343 mg, 28%) as an oil followed by 3-*epi*-**30** (385 mg, 32%) as an oil.

30: ν_{max} (cm^{-1}) 3468, 2947, 2873, 1772, 1738, 1454, 1367, 1275, 1199, 1163, 1095, 1062, 1016, 917, 880, 736, 698. δ_H (300 MHz; CDCl$_3$) 1.58–2.24 (13 H, m), 2.45 (1 H, m, H-13), 2.83 (1 H, d, *J* 10.4, H-6), 3.54 (1 H, d, *J* 10.6, H-5), 3.59–3.62 (4 H, m, H-18 and –CO$_2$CH$_3$), 3.97 (1 H, d, *J* 10.0, H′-18), 4.16 (1 H, m, H-3), 4.45 (1 H, d, *J* 11.9, H-1′), 4.47 (1 H, d, *J* 11.7, H′-1′), 7.26–7.39 (5 H, m, H-2″–H-6″). δ_C (75 MHz; CDCl$_3$) 16.9 (C-11), 25.0 (C-12), 27.2 (C-1 and C-2), 35.0 (C-14), 44.9 (C-13), 50.0 (C-9), 50.1 (C-15), 50.8 (C-8), 52.1 (C-6), 52.7 (–CO$_2$*C*H$_3$), 53.6 (C-5), 57.9 (C-4), 70.3 (C-3), 71.6 (C-18), 74.2 (C-1′), 95.4 (C-10), 127.6 (C-4″), 128.1 (C-2″ and C-6″), 128.5 (C-3″ and C-5″), 136.4 (C-1″), 172.1 (C-19), 174.8 (C-7), 219.8 (C-16). *m*/*z* (ESI) 478 (8%), 477 (19), 455 (10), 333 (4), 241 (4), 178 (8), 162 (32), 160 (43), 156 (81), 153 (100), 102 (16). HRMS (EI) calcd for M$^+$, C$_{26}$H$_{30}$O$_7$: 454.1991; found: 454.1987.

3-*epi*-30. ν_{max} (cm^{-1}) 3468, 2949, 2837, 1770, 1738, 1496, 1454, 1437, 1366, 1273, 1197, 1175, 1097, 1057, 1027, 975, 916, 885, 813, 734, 698. δ_H (300 MHz; CDCl$_3$) 1.45–2.27 (14 H, m), 2.73 (1 H, d, *J* 10.1, H-6), 3.01 (1 H, d, *J* 10.1, H-5), 3.54 (3 H, s, –CO$_2$CH$_3$), 3.69 (1 H, d, *J* 10.1, H-18), 3.92 (1 H, d, *J* 10.1, H′-18), 4.01 (1 H, m, H-3), 4.43 (1 H, d, *J* 11.9, H-1′), 4.49 (1 H, d, *J* 12.0, H′-1′), 7.25–7.38 (5 H, m, H-2″–H-6″). δ_C (75 MHz; CDCl$_3$) 16.9 (C-11), 25.1 (C-12), 28.9 and 29.8 (C-1 and C-2), 35.1 (C-14), 44.8 (C-13), 50.6 (C-15), 50.9 (C-8), 52.0 (C-9), 52.8 (–CO$_2$*C*H$_3$), 53.1 (C-6), 55.0 (C-5), 58.6 (C-4), 66.5 (C-18), 69.8 (C-3), 73.6 (C-1′), 94.5 (C-10), 127.4 (C-4″), 127.7 (C-2″ and C-6″), 128.3 (C-3″ and C-5″), 137.4 (C-1″), 172.2 (C-19), 174.5 (C-7), 219.9 (C-16). *m*/*z* (ESI) 477 (8%), 472 (11), 456 (23), 455 (100), 437 (7), 423 (22), 407 (5), 347 (7), 156 (13). HRMS (EI) calcd for M$^+$, C$_{26}$H$_{30}$O$_7$: 454.1991; found: 454.1988.

Equilibration of *ent*-18-Benzyloxy-3β,10β-dihydroxy-16-oxo-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester 19,10-lactone (3-*epi*-30)

To a stirred solution of 3-*epi*-**30** (174 mg, 0.383 mmol) in benzyl alcohol (1.25 mL) was added DBU (575 μL, 3.83 mmol). After 2 h, this was poured into 1.0 M HCl (5 mL) and extracted with 5% 2-butanol in EtOAc (3 × 10 mL). The organic layers were washed with water (2 × 7.5 mL), and the combined aqueous extracts were then back-extracted with 5% 2-butanol in EtOAc (2 × 5 mL). The combined organic layers were washed with brine (20 mL) and dried (MgSO$_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 9, increasing to 3 : 2) to afford **30** (70 mg, 40%) as an oil followed by 3-*epi*-**30** (103 mg, 59%), also as an oil.

ent-16-Oxo-3α,10β,18-trihydroxy-17,20-dinorgibberellane-7,19-dioic acid 7-methyl ester
19,10-lactone

A stirred solution of **30** (196 mg, 0.43 mmol) in EtOAc (20 mL) was treated with 10% palladium hydroxide on charcoal, and the resulting mixture was stirred for 72 h under an atmosphere of hydrogen. The suspension was then filtered through Celite, and the filtrate was concentrated *in vacuo* to afford the title compound (157 mg, 100%) as a white foam. ν_{max} (cm^{-1}) 3468, 2950, 2875, 1767, 1737, 1437, 1383, 1280, 1199, 1163, 1117, 1087, 1060, 1015, 986, 918, 883, 806, 754. δ_H (300 MHz; CDCl$_3$) 1.62–2.13 (13 H, m), 2.46 (1 H, m, H-13), 2.90 (1 H, d, *J* 11.1, H-6), 3.38 (1 H, d, *J* 11.3, H-5), 3.70 (1 H, d, *J* 12.5, H-18), 3.80 (3 H, s, $-CO_2CH_3$), 4.03 (1 H, d, *J* 12.8, H′-18), 4.31 (1 H, d, *J* 1.9, H-3). δ_C (75 MHz; $CDCl_3$) 17.0 (C-11), 25.1 (C-12), 27.3 and 27.3 (C-1 and C-2), 34.2 (C-14), 44.4 (C-13), 48.2 (C-9), 49.4 (C-8), 50.0 (C-15), 51.9 (C-6), 52.9 ($-CO_2CH_3$), 54.3 (C-5), 58.3 (C-4), 64.3 (C-18), 70.4 (C-3), 94.0 (C-10), 174.1 and 174.7 (C-7 and C-19), 219.8 (C-16). *m/z* (EI) 364.1522 ($C_{19}H_{24}O_7$ M^+ requires 364.1522), 347 (9), 336 (95), 314 (35), 300 (76), 286 (100), 272 (44), 258 (57), 242 (43), 228 (32), 214 (24), 201 (18), 181 (15), 169 (20), 157 (25), 143 (22), 129 (33), 117 (23), 105 (24).

ent-10β-Hydroxy-3α,18-bis-tetrahydropyranyloxy-20-norgibberell-16-ene-7,19-dioic acid 7-methyl ester 19,10-lactone (31)

To a stirred solution of the diol prepared above (157 mg, 0.432 mmol) in CH_2Cl_2 (5 mL) was added PPTS (54 mg, 0.216 mmol) and dihydropyran (394 μL, 4.32 mmol). After 16 h, the reaction was diluted with EtOAc (20 mL), washed with brine (120 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 2) afforded **31** (230 mg, 100%) as an oil. ν_{max} (cm^{-1}) 3469, 2945, 2873, 2249, 1777, 1741, 1454, 1439, 1384, 1351, 1279, 1258, 1200, 1163, 1122, 1075, 1034, 993, 966, 911, 870, 814, 731. δ_H (300 MHz; $CDCl_3$) 1.47–2.16 (80 H, m), 2.43 (4 H, m, H-13), 3.14–3.64 (20 H, m), 3.66 (3 H, s, $-CO_2CH_3$), 3.67 (3 H, s, $-CO_2CH_3$), 3.70 (3 H, s, $-CO_2CH_3$), 3.71 (3 H, s, $-CO_2CH_3$), 3.74–4.17 (16 H, m), 4.52–4.69 (6 H, m, THP-H1), 4.82 (1 H, m, THP-H1), 4.94 (1 H, m, THP-H1). δ_C (75 MHz; $CDCl_3$) 16.9, 18.4, 19.4, 19.6, 19.7, 19.9, 20.1, 20.3, 22.8, 22.9, 25.2, 25.4, 25.4, 25.5, 26.7, 26.8, 27.9, 28.3, 29.2, 29.8, 30.4, 30.6, 30.8, 30.9, 31.0, 31.1, 32.0, 34.4, 44.6, 49.8, 49.9, 50.1, 50.1, 50.4, 51.6, 51.8, 52.6, 52.8, 53.6, 57.8, 58.4, 58.5, 59.1, 60.7, 60.9, 62.0, 62.5, 62.7, 63.0, 63.6, 63.8, 65.4, 65.9, 67.0, 67.4, 69.5, 69.7, 75.2, 75.5, 93.0, 93.2, 93.3, 93.6, 94.6, 95.2, 95.2, 97.2, 97.5, 98.9, 100.5, 100.6, 101.8, 101.9, 172.3 (C-19), 172.5 (C-19), 175.0 (C-7), 175.5 (C-7), 220.7 (C-16), 220.8 (C-16). *m/z* (EI) 501.2492 ($C_{28}H_{37}O_8$ requires 501.2488) 532 (M^+, 1%), 501 (2), 447 (12), 430 (5), 414 (3), 375 (3), 364 (39), 336 (11), 315 (19), 286 (18), 269 (11), 257 (14), 243 (8), 225 (16), 201 (6), 185 (10), 155 (8), 129 (7), 101 (26), 93 (8), 85 (100), 57 (12).

ent-3α,18-Bis-tetrahydropyranyloxy-10β-hydroxy-20-norgibberell-16-ene-7,19-dioic acid 7-methyl ester 19,10-lactone

To a stirred suspension of triphenylmethylphosphonium iodide (699 mg, 1.73 mmol) in THF (5 mL) at −78 °C was added 1.0 M NaHMDS in THF (1.5 mL, 1.50 mmol). This mixture was allowed to warm to rt and stirred for 1 h, forming a bright yellow solution. To a stirred solution of **31** (230 mg, 0.432 mmol) in THF (5 mL) at −78 °C was added slowly *via* a gas-tight syringe the ylide solution (2.5 mL, 0.592 mmol) prepared above. After 1 h, the reaction was allowed to warm slowly to rt over 1 h. After a further 2 h, the reaction was cooled to −78 °C and a second addition of the ylide solution (1.6 mL, 0.389 mmol) was made. After 30 min, the reaction was allowed to warm to rt, and after a further 45 min was quenched with saturated aqueous NH_4Cl solution (20 mL). The reaction mixture was extracted with EtOAc (3 × 15 mL), and the combined organic layers were then washed with water (3 × 15 mL). The combined aqueous layers were back-extracted with EtOAc (2 × 15 mL), and the combined organic layers were then washed with brine (50 mL) and dried ($MgSO_4$). Concentration *in vacuo* and column chromatography on silica (EtOAc–hexane 1 : 3) afforded the title compound (175 mg, 76%) as a white foam. ν_{max} (cm^{-1}) 3469, 2943, 2873, 1775, 1735, 1655, 1454, 1436, 1384, 1350, 1278, 1199, 1171, 1123, 1074, 1034, 993, 966, 910, 871, 813. δ_H (300 MHz; $CDCl_3$) 1.34–2.14 (100 H, m), 2.64 (4 H, m, H-13), 3.07–3.21 (4 H, m, H-6), 3.32–3.43 (4 H, m, H-5), 3.46–3.60 (12 H, m), 3.64 (3 H, s, $-CO_2CH_3$), 3.64 (3 H, s, $-CO_2CH_3$), 3.68 (3 H, s, $-CO_2CH_3$), 3.69 (3 H, s, $-CO_2CH_3$), 3.70–4.15 (16 H, m), 4.54–4.70 (7 H, m, THP-H1), 4.80–4.84 (5 H, m, H-17 + THP-H1), 4.97 (4 H, s, H′-17). δ_C (75 MHz; $CDCl_3$) 16.3, 18.4, 19.3, 19.4, 19.6, 19.9, 20.1, 20.2, 22.8, 22.8, 25.3, 25.4, 25.5, 26.8, 26.9, 27.3, 28.2, 28.3, 28.6, 29.8, 30.4, 30.8, 30.9, 31.1, 31.8, 32.0, 36.4, 37.4, 38.6, 38.6, 39.1, 44.4, 44.6, 49.9, 50.1, 50.2, 51.4, 51.4, 51.5, 51.5, 51.8, 53.2, 57.5, 57.6, 58.3, 58.3, 60.0, 60.7, 60.9, 62.3, 62.6, 62.7, 63.0, 63.4, 63.8, 65.4, 66.0, 66.9, 67.5, 68.3, 69.6, 69.8, 70.6, 75.6, 77.2, 93.3, 93.6, 93.7, 94.0, 94.3, 94.6, 95.0, 95.8, 97.2, 97.4, 99.4, 100.4, 100.5, 101.7, 101.8, 107.3 (C-17), 156.4 (C-16), 157.5 (C-16), 157.5 (C-16), 157.6 (C-16), 162.1, 173.0 (C-19), 173.1 (C-19), 175.4 (C-7), 175.8 (C-7). *m/z* (EI) 560 (1%), 530 (1), 499 (1), 479 (1), 460 (1), 445 (2), 428 (2), 415 (2), 402 (2), 376 (7), 362 (49), 344 (6), 312 (19), 298 (6), 284 (20), 267 (11), 254 (12), 240 (10), 223 (26), 181 (9), 155 (10), 142 (8), 129 (11), 116 (6), 105 (9), 85 (100), 67 (27), 57 (33). HRMS (FAB) *m/z* calcd for M + Na^+, $C_{30}H_{42}O_8Na$: 553.2777; found: 553.2777.

ent-3α,10β,18-Trihydroxy-20-norgibberell-16-ene-7,19-dioic acid 19,10-lactone (3)

To a stirred, degassed suspension of NaH (240 mg, 10 mmol) in HMPA (5 mL) was added dropwise freshly distilled propane thiol (0.7 mL, 7.72 mmol), and the mixture stirred for 2 h then left to stand for 1 h. To a stirred solution of the protected ester prepared above (155 mg, 0.292 mmol) in HMPA (1 mL) was added the thiolate solution (0.68 mL, 1.02 mmol). After 16 h, the reaction mixture was diluted with water (7.5 mL), acidified to pH 3 with cold 2.0 M HCl and then extracted with 20% 2-butanol in EtOAc (3 × 10 mL). The combined organic layers were washed to pH 4.5 with KH_2PO_4, then washed with $CuCl_2$ solution (2 × 4 mL), back-extracting each time with 20% 2-butanol in EtOAc. The combined organic layers were then washed with brine (20 mL) and dried ($MgSO_4$). Concentration *in vacuo* and chromatography through a short column of silica (EtOAc–hexane 3 : 1) gave the crude carboxylic acid (123 mg, 81%) as an oil. To a stirred solution of the crude carboxylic acid (38 mg, 0.0736 mmol) in EtOH (3 mL) was added PPTS (4 mg, 0.0147 mmol). After 1 h, the reaction was warmed to 57 °C, and after a further 6 h was cooled to rt and concentrated *in vacuo*. The resulting residue was taken up in EtOAc (5 mL), washed with brine–water 3 : 1 (3 mL) and then dried ($MgSO_4$). Concentration *in vacuo* afforded **3** (24 mg, 92%) as a white solid, which was further purified by reverse-phase HPLC on C-18 stationary phase (45% acetonitrile and 55% water containing 0.1% acetic acid). Mp 178–180 °C. ν_{max} (cm^{-1}) 3401, 2931, 1752, 1713, 1658, 1453, 1415, 1318, 1261, 1198, 1163, 1099, 1067, 1016, 988, 925, 886, 810, 754. δ_H (300 MHz; $CDCl_3$) 1.21–2.21 (13 H, m), 2.67 (1 H, m, H-13), 2.89 (1 H, d, *J* 11.1, H-6), 3.32 (1 H, d, *J* 11.1, H-5), 3.79 (1 H, m, H-18), 4.00 (1 H, d, *J* 12.3, H′-18), 4.29 (1 H, s, H-3), 4.89 (1 H, s, H-17), 5.01 (1 H, s, H′-17).

δ_C (75 MHz; $CDCl_3$) 16.3 (C-11), 27.5 and 27.6 (C-1 and C-2), 31.5 (C-12), 36.4 (C-14), 38.6 (C-13), 44.0 (C-15), 48.7 (C-9), 50.8 (C-6), 51.2 (C-8), 53.6 (C-5), 58.2 (C-4), 63.3 (C-18), 69.3 (C-3), 95.1 (C-10), 107.9 (C-17), 156.5 (C-16), 175.9 (C-19), 176.8 (C-7). *m*/*z* (EI) 348.1576 (M^+ $C_{19}H_{24}O_6$ requires 348.1573), 330 (67), 312 (100), 302 (23), 284 (54), 268 (29), 254 (57), 240 (43), 227 (23), 214 (39), 197 (17), 181 (18), 171 (22), 157 (20), 141 (22), 129 (26), 115 (20), 105 (21), 91 (49), 77 (28), 61 (22). Me-TMSi: *m*/*z* (EI) 506 (7), 491 (35), 488 (35), 474 (63), 384 (57), 378 (43), 369 (60), 356 (40), 341 (70), 317 (100), 308 (37), 294 (70), 281 (50), 266 (68), 223 (72), 221 (48), 155 (29), 129 (23).

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